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Study of binocular visual performance inducing visual quality deterioration under different experimental conditions: influence on driving

Estudio del rendimiento visual binocular tras inducir un deterioro en la calidad visual bajo condiciones experimentales diversas: influencia en la conducción

Tesis Doctoral/ Doctoral Thesis

Memoria de Doctorado

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CONTENTS

ABSTRACT

In our daily tasks, vision plays a paramount role in our perception. Indeed, binocular vision represents an important part in information processing. Through this process, an important achievement is represented by the combination of these two monocular images in a single one allowing a normal binocular vision. This ensuing binocular image provides several advantages in our visual perception compared to the monocular one, since allow us get a greater visual field but also having stereoscopic perception (depth perception), resulting in an improvement of visual performance. In the field of study of visual performance, most of the works focused on the monocular vision assessment even if vision is mostly binocular. So, it arises the importance to assess binocular visual performance on visual function through the measurements of different visual parameters such as visual acuity, contrast sensitivity and stereopsis. To optimize binocular vision performance, it is important to limit as much as possible any difference between the two eyes in order to obtain a suitable binocular balance. However, binocular visual performance can be easily affected to a greater or lesser degree of ocular impairment. Moreover, deteriorations in binocular visual performance can emerge even after some types of ocular surgery causing binocularly discomfort and reduction in their visual quality, due to a potential increase of intraocular scattering and ocular aberrations. Another important involvement in deterioration of binocular visual performance can emerge in ocular pathologies such as cataract which could affect firstly in one eye causing an ocular imbalance and interocular differences. In these pathologies, a progressive degradation in ocular (optical quality and straylight) and visual (such as visual acuity, contrast sensitivity and stereopsis) parameters alters binocular visual performance.

Different experimental conditions could also affect binocular visual performance impacting strongly its efficiency. One of this condition is alcohol consumption. Alcohol represents the most common psychoactive substance consumed in the world. It inhibits the correct information processing of nervous system. Alcohol and vision have been widely assessed through the years showing that depending on the visual function studied, ingested alcohol content can impact and deteriorate differently visual function. However, there is a lack of investigation concerning the influence of a moderate alcohol consumption on binocular visual performance taking in consideration not only visual acuity, but also stereopsis and the

vergence system, and how could affect some daily tasks such as driving. With the importance of binocular vision and its impairment caused by alcohol consumption, a complex task as driving is negatively affected being a prevalent cause in traffic accidents.

Taking into account all these considerations, the main objective of this Doctoral Thesis was to assess how visual quality deteriorations impact on monocular and binocular visual performance under different experimental conditions and to analyze the impact of binocular vision after alcohol consumption on a daily task such as driving. In that respect, the Doctoral Thesis was divided in four studies. The first was dedicated to assess monocular visual performance after the deterioration of retinal image quality after inducing forward scattering. Related to the first study, the second one analyzed the effect of interocular differences on binocular visual performance due to induced forward scattering. The third work was designed to study how defocus and pupil size influence binocular summation and the last one analyzed how deterioration of binocular vision after a moderate alcohol intake influences driving performance, using for this purpose a driving simulator.

Monocularly, our results revealed that by inducing forward scattering, the greater the retinal-image degradation, the stronger the visual performance impairment, finding a positive correlation between forward scattering and night-vision disturbances (study 1). Binocularly, the increased forward scattering induced on the dominant eye resulted in higher interocular differences, which jeopardized overall binocular visual performance: the greater the interocular differences in the ocular parameters, the lower the binocular summation of the visual functions and the poorer the stereoacuity at distance (study 2). Under the effect of defocus in combination with control of the pupil size, we observed a better binocular summation with higher defocus and lower contrast induced in visual acuity due to its neural factor and not only to its optical one, showing the binocular summation benefits of similar monocular conditions, such as pupil size (study 3). Lastly, some binocular visual functions and vergence system deteriorated after alcohol consumption and correlated with simulated driving impairment, which indicates that the deterioration of binocular vision due to a moderate alcohol consumption affects driving, thus could reduce road safety (study 4).

RESUMEN

En el desarrollo de nuestras tareas diarias, la visión juega un papel esencial en nuestra percepción. De hecho, la visión binocular representa una parte esencial en el procesamiento de la información. A través del proceso de la visión binocular, las dos imágenes monoculares se combinan en la corteza visual permitiendo generar la percepción de una única imagen que contiene mayor información. Esta percepción única proporciona diversas ventajas respecto a las imágenes monoculares, ya que, no sólo aumenta el campo visual y mejoran algunas funciones visuales, sino que se consigue la percepción estereoscópica (percepción de la profundidad), resultando en una mejora del rendimiento visual. En el campo de estudio de este rendimiento visual, la mayoría de trabajos se centran en la evaluación de la visión monocular a pesar de que nuestra visión es binocular en condiciones normales. Sin embargo, es importante la evaluación, no sólo de la visión monocular a través de funciones visuales como la agudeza visual o la sensibilidad al contraste, sino también de la visión binocular a través de estas mismas funciones y de otras como la estereopsis, el sistema vergencial o la sumación binocular. La existencia de diferencias entre ambos ojos puede afectar a la eficacia de la visión binocular, por lo que se podría optimizar esta eficacia reduciendo esas diferencias interoculares. Por otro lado, el rendimiento visual puede verse afectado por el deterioro ocular. Es más, la visión binocular puede verse afectada incluso tras algunos tipos de cirugía ocular causando deterioro en la calidad de la visión y disconfort visual, todo ello debido a un posible aumento de la difusión luminosa intraocular, de las aberraciones oculares o del aumento de las diferencias interoculares. El deterioro de la visión binocular también puede deberse a diversas patologías oculares como las cataratas, que pueden afectar primeramente a un ojo, produciendo no sólo alteración de la visión en un ojo, sino generando además diferencias interoculares. En estas patologías, el deterioro progresivo en parámetros oculares (calidad óptica ocular) y visuales (tales como la agudeza visual, la sensibilidad al contraste o la estereopsis) altera el rendimiento de la visión binocular.

Las condiciones experimentales también pueden afectar a la eficacia de la visión binocular. Una de las condiciones que pueden mermar esta eficacia es el consumo de sustancias como el alcohol. El alcohol representa la sustancia psicoactiva consumida más frecuente a nivel mundial. Inhibe el procesamiento de la información del sistema nervioso. De hecho, el consumo de alcohol y su influencia en la visión han sido ampliamente estudiados a lo largo de los años mostrando que, dependiendo de la función visual

analizada, el contenido de alcohol ingerido puede impactar y deteriorar de forma distinta la función visual. Sin embargo, hay carencia de trabajos que analicen la influencia de un consumo moderado de alcohol en el rendimiento visual binocular de una manera completa, teniendo en cuenta funciones como la agudeza visual, la estereopsis y el sistema vergencial y cómo puede afectar a determinadas tareas cotidianas como la conducción. En este sentido, el deterioro que la visión binocular puede sufrir tras consumo de alcohol podría afectar negativamente a una tarea compleja como la conducción, siendo, además, este consumo de alcohol, una causa de prevalencia en accidentes de tráfico.

Teniendo en cuenta todas estas consideraciones, el principal objetivo de esta Tesis Doctoral es evaluar cómo el deterioro de la calidad visual afecta al rendimiento visual monocular y binocular bajo diferentes condiciones experimentales y analizar el impacto de la visión binocular tras consumo de alcohol en una tarea diaria como la conducción. Para ello, la tesis doctoral está dividida en cuatro estudios. El primero de ellos se centra en evaluar el rendimiento visual monocular tras el deterioro de la calidad de imagen retiniana que se obtiene tras inducir difusión luminosa intraocular con el uso de filtros. En relación con este primer estudio, el segundo analiza el rendimiento visual binocular en presencia de diferencias interoculares, obtenidas tras inducir difusión luminosa monocularmente. El tercer trabajo estudia cómo el desenfoque y el tamaño pupilar afectan a la sumación binocular. El último estudio analiza cómo el deterioro de la visión binocular tras consumo de alcohol afecta al rendimiento en la conducción, usando para ello un simulador de conducción.

Monocularmente, los resultados muestran que, tras inducir difusión luminosa intraocular, cuanto mayor es la degradación de la imagen retiniana debido a esa difusión luminosa intraocular, mayor es el deterioro en el rendimiento visual monocular, encontrándose además una correlación positiva entre la difusión luminosa intraocular y las alteraciones de la visión nocturna (estudio 1). Binocularmente, el aumento de la difusión luminosa en el ojo dominante produce un aumento en las diferencias interoculares de diversos parámetros oculares, lo que afecta negativamente al rendimiento visual binocular de modo que cuanto mayores son esas diferencias interoculares más baja es la sumación binocular y peor la estereopsis en visión lejana (estudio 2). En el caso de un desenfoque binocular controlando el tamaño de la pupila, se observa una mejor sumación binocular para un mayor desenfoque y contraste más bajo, predominando en este caso el efecto de factores neuronales frente a ópticos, lo que muestra los beneficios en la sumación binocular cuando existen condiciones monoculares similares, como el tamaño de pupila (estudio 3). Finalmente se obtiene que algunas funciones visuales binoculares y el sistema vergencial se deterioran tras consumo de alcohol y además este deterioro está correlacionado con un empeoramiento de las variables de conducción en el simulador. Esto indica que el deterioro en la visión binocular tras consumo de alcohol afecta al rendimiento en la conducción y, por tanto, podría afectar a la seguridad del tráfico (estudio 4).

CHAPTER 1

INTRODUCTION

In our daily tasks, vision plays a paramount role in our perception. Indeed, binocular vision represents an important part in information processing. To this end, light entering in the pupil from each eye passes through the various ocular structures until retina where light changes in electric impulse to be analyzed by visual cortex. Through this process, an important achievement is represented by the combination of these two monocular images (from the right and the left eye) in a single one allowing a normal binocular vision. This ensuing binocular image provides several advantages respect to the monocular one, since stereoscopic perception and a greater visual field are achieved, resulting in a better visual performance and, therefore, a better relationship with the environment. Regarding visual performance, most of the works have focused on the monocular vision assessment even if, as it is well established, normal vision is under binocular conditions. So, taking into account these considerations, it arises the importance to assess binocular visual performance through the measurements of different visual parameters such as visual acuity, contrast sensitivity, stereopsis, etc. However, some factors such as interocular differences in higher-order aberrations can inherently limit the optimization of binocular vision performance. Binocular visual performance can be easily affected to a greater or lesser degree of impairment. One of the most common cause is due to asthenopia which is defined as eyestrain. It is accompanied by several symptoms as eye pain, dry eyes, eye swelling, ocular fatigue, blurry vision, photophobia, discomfort, lacrimation and headaches arising usually from a prolonged visual effort at near and an uncorrected refractive error. For instance, population could be easily affected by one of these symptoms as it occurs in a large part of university students (Han et al., 2013; Yekta et al., 2017). Moreover, deteriorations in binocular visual performance can be provided even after an ocular surgery for correcting an ametropia such as keratotomy (Krasnov et al., 1988; Ginsburg et al., 1990; Applegate et al., 1998) or laser-assisted in situ keratomileusis, LASIK (Villa et al., 2009; Anera et al., 2011) which is one of the most common surgery practicing. In these surgeries, patients can suffer binocularly discomfort and reduction in their visual quality due to higher intraocular scattering, glare and ocular aberrations (Villa et al., 2009; Alarcon et al., 2011).

Another important involvement in deterioration for binocular visual performance can emerge in ocular pathologies which could affect firstly in one eye causing an ocular imbalance between the two eyes or directly, in both eyes. Deteriorations affecting firstly one eye may be the case for several ocular pathologies such as cataract (Gothwal et al., 2009; Olson et al., 2017), age-related macular degeneration (Midena et al., 1997; Bellmann et al., 2003; Ortiz et al., 2010) and, by definition, amblyopia (Holopigian et al., 1988; Holmes and Clarke, 2006). Indeed, in most cases of unilateral cataract (affecting only one eye), patients suffer a progressive degradation and lost in visual functions (such as visual acuity and contrast sensitivity) in this eye inducing a decrease in binocular visual performance. In case of amblyopia, amblyopic eye is characterized by a lower visual acuity compared to non-amblyopic one inducing ocular imbalance between the two eyes and, altering binocular visual performance.

With this keep in mind, it results an important issue to study how an impairment in one eye, with a consequent increment in the interocular differences, can affect binocular visual performance since this can happen with ocular pathologies stated above but also after cataract or corneal refractive surgery. For this purpose, different simulated penalizations can be achieved through different filters or with the addition of various degrees of positive lenses (spherical and cylindrical) inducing blurring retinal image.

Regarding filters, Bangerter foils have been widely used in the therapy of amblyopia penalizing the eye with better visual acuity (Iacobucci et al., 2001) being able to control the visual acuity required. Therefore, the wide range of Bangerter foils can allow us to simulate different degrees of monocular penalization for ocular and visual parameters. In addition, others filters as BPM2 filter can simulate an early cataract (de Wit et al., 2006) affecting less visual acuity than Bangerter foils. Different levels of monocular impairment could be induced with these filters placed in one eye and, therefore, a wide range of interocular differences could be achieved, which would allow to analyze the influence of these monocular deteriorations on binocular visual performance.

So, in order to evaluate a complete framework of the binocular visual performance taking into account monocular penalization, several visual parameters can be studied including visual acuity, contrast sensitivity and stereopsis, but also, several ocular parameters such as optical quality and straylight. As it is well established, visual acuity represents the most common visual function measured which gives a first important data to assess visual function. However, other visual functions should not be ignored, especially when they directly characterize binocular vision. In this sense, stereopsis is the highest level of binocular vision allowing depth vision. The evaluation of this visual attribute provides an important and valid measurement in binocular visual performance. To ensure a steady stereopsis and, in consequence, normal binocular vision, fusional reserves have to compensate horizontal and vertical phorias at distance and near. In the assessment of the binocular visual performance, it is important to consider ocular parameters and monocular visual function and to analyze how these interocular differences may affect this performance. With this in mind, the study of both monocular and binocular function can allow to characterize the efficiency of binocular vision through, for instance, binocular summation (Home, 1978;

Frisen and Lindblom, 1988). In addition, the study of various ocular parameters allows to quantify these interocular differences and how they influence binocular visual performance. Among these, studies have investigated the influence of interocular differences in ocular aberrations and in ocular optical quality on binocular visual performance (Jimenez et al., 2007; Jimenez et al., 2008b; Castro et al., 2009). So, another important assessment to achieve is represented by optical quality with the quantification of intraocular scattering which is defined by the quantity of light entering in each eye through the pupil varying the contrast of the image and inducing straylight. Due to the importance in monocular optical quality, all these parameters might help to quantify binocular visual performance. Thus, all these visual and ocular parameters associated with the wide range of monocular penalization could permit us to interpret better how binocular visual performance changes.

On the other hand, different experimental conditions could also affect binocular visual performance impacting strongly its efficiency. One of this condition is alcohol consumption. It results of interest to investigate how alcohol consumption may disrupt the correct binocular visual performance knowing that alcohol is widely consumed and integrated in ours societies (WHO, 2018). Depending of the quantity of alcohol ingested and the corresponding breath alcohol content obtained, alcohol consumption can damage tragically our lives. According to the World Health Organization (WHO) and its Global Information System on Alcohol and Health (GISAH), more than 3 million people died as a result of harmful alcohol use in 2016 (WHO, 2018), which represents 1 in 20 deaths worldwide. It represents the most common psychoactive substance consumed in the world. It inhibits the correct processing of nervous system. Alcohol and vision have been widely studied through the years showing that depending on the visual function studied, alcohol content ingested can impact and deteriorate differently visual function (Wilkinson et al., 1974; Wilson and Mitchell, 1983; Nicholson et al., 1995) and subsequently, visual performance which can induce diplopia from a certain level of moderate-high alcohol ingested (Charnwood, 1950; Brecher et al., 1955). For instance, visual acuity and stereoacuity could need higher quantity of alcohol consumed to be strongly impaired (Seedorff, 1956) respect to visual functions such as visual field, accommodation and convergence which seem to be more sensitive (Hill and Toffolon, 1990; Watten and Lie, 1996). Regarding visual acuity and stereoacuity at far, a lack of investigation exists concerning these visual parameters under the effects of a moderate alcohol consumption and how it influences in daily tasks. Even if alcohol and vision have been investigated to some visual parameters, there is a lack of study which investigate in wholly the influence of alcohol on binocular visual performance that is, for instance, taking into consideration visual acuity, stereopsis and the vergence system. In addition, alcohol and vision is an extensive issue which depends of several external factors as age, weight, gender and quantity of alcohol ingested which makes it even more difficult to compare the findings of different studies between them and in consequence, results cannot be generalized.

So, with the importance of binocular vision and its impairment due to alcohol consumption, it could be of interest to understand how alcohol and binocular visual performance affect concretely our daily visual tasks such as driving. Driving represents a complex task requiring controlled behavior as speed, braking, lane position, reaction time (Allen et al., 1975) but also, attention, concentration and high processing qualities through the central nervous system. Alcohol intake is a prevalent factor in road traffic deaths. As it is well established, driving and alcohol constitute a hazardous combination (Reading and Hofstetter, 1969). Indeed, according to National Department of Traffic (NDT), driving under the influence of alcohol represents the highest incidence of traffic accidents in the European Union (31%) while in the United States of America (USA), over 1,000 college students die each year in an alcohol-related accident (Hingson et al., 2014). Even if in the majority of the world countries, the maximum breath alcohol content (BrAC) established for driving is a blood alcohol content (BAC) equivalent to 0.05%, there still are forty-five countries like USA or United Kingdom authorizing blood alcohol content equivalent to 0.08%. On the other hand, to obtain a driving license, in most of the countries, visual requirements are a binocular visual acuity equal or greater than 0.5 (in decimal notation) or a monocular visual acuity equal or superior to 0.6 (International Council of Ophtalmology, 2006) and a normal visual field (Owsley and McGwin, 2010). However, several researches pointed out that for instance, only visual acuity is not a sufficient visual parameter which can predict a quality of vision and a safe driving (Wood and Owsley, 2005; Owsley and McGwin, 2010; Wood and Owsley, 2016). In these circumstances, they suggested to take into account other visual functions as contrast sensitivity (Owsley et al., 2015), glare disability (Babizhayev, 2003) or stereoacuity (Maag et al., 1997). Regarding the latter, it has been disclosed that a good stereoacuity improved significantly the number and the severity of collisions (Maag et al., 1997; Rubin et al., 2007). Thereby, it is important to assess how driving under the effects of a legal limit of alcohol (as BAC of 0.08%) could affect and correlate binocular visual performance in terms of visual acuity, stereoacuity, phorias and fusional reserves in a young drivers' population.

Taking into account all these considerations, the present work has been designed to assess different kind of visual deteriorations in order to understand the impact on binocular visual performance. Indeed, many studies regarding this impairment of vision have been done. Nevertheless, these researches did not investigate a full framework of ocular parameters and visual functions including a wide and variable range of interocular differences to understand the behavior of binocular vision. The influence of vision impairment due to alcohol on driving is also part of this work. Thereby, binocular summation for different visual functions and stereopsis could be suitable metrics to analyze binocular visual performance under different degrees of interocular differences (Jimenez et al., 2008b; Castro et al., 2017). In addition, the control of pupil diameter is an important factor to consider in binocular visual performance since it determines the quantity of light entering in eyes and consequently, the intraocular scattering. So, it could allow to verify how binocular summation is affected by monocular deterioration.

In that respect, the research work presented in this doctoral thesis is structured as follows:

- **Chapter 2** is dedicated to the literature review on the different aspects discussed in this doctoral thesis. Above all, fundamental and theoretical aspects in the binocular vision are treated as its visual pathway organization and the visual mechanisms responsible to the binocular vision. Thus, we describe the theoretical impact of interocular differences on binocular vision. We include a review examining monocular and binocular visual deterioration in different visual parameters such as visual acuity, contrast sensitivity, stereopsis, phorias, fusional reserves, light scattering and optical quality. Finally, we review about the influence of alcohol on binocular vision and driving impairment.

- **Chapter 3** represents our first study which deals with monocular visual performance after the deterioration of retinal image quality inducing forward scattering using Bangerter foils and fog filters. We induced and evaluated different levels of monocular retinal-image degradation assessed by means of visual acuity, contrast threshold, straylight and visual discrimination capacity.

- **Chapter 4** details our second study which assesses binocular visual performance by means of stereoacuity and binocular summation for different visual functions (visual acuity, contrast sensitivity and visual disturbances) after inducing monocular forward scattering (by Bangerter foils and fog filters placed on the dominant eye). This study allows to analyze how the binocular visual performance is influenced by the interocular differences induced taking into consideration various ocular parameters, such as the Objective Scatter Index (OSI), the Strehl ratio (SR), or the straylight (log(s)).

- **Chapter 5** describes our third study which shows the impact of the pupil size on high and low contrast distance visual acuity and light disturbance in young healthy eyes undergoing different levels of defocus (spherical and cylindrical positive lenses additions) and to investigate the influence of binocular summation under two pupil size conditions (3 and 5 mm).

- **Chapter 6** provides our fourth study which checks out the influence of moderate alcohol intake (breath alcohol content equivalent to 0.40 mg/l) on binocular vision, vergence system and simulated driving performance by analyzing the interactions between visual deterioration and driving variables. For the analysis, we evaluated visual functions such as visual acuity, stereoacuity, phorias, fusional reserves, and vergence facility. In addition, we checked the Sheard's and Percival's criteria at near and we calculated the accommodative convergence/accommodation (AC/A) ratio.

- Finally, **Chapter 7** highlights the conclusions drawn from the different studies of this doctoral thesis. We also describe future work related to the content of this doctoral thesis.

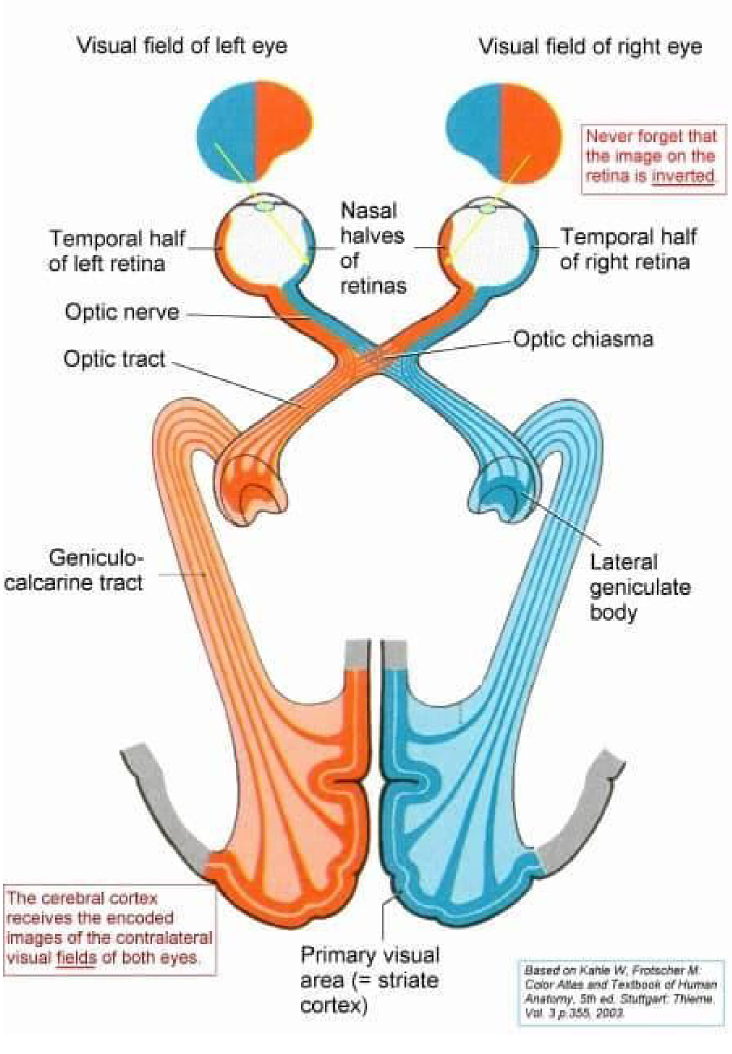
CHAPTER 2

LITERATURE REVIEW

2.1. FUNDAMENTAL ASPECTS IN THE BINOCULAR VISION

2.1.1. Visual pathways

To perceive an image of our surroundings, the light energy entering through the pupil of each eye passes through the different ocular structures such as cornea, aqueous humor, lens and vitreous humor ending on the retina of each eye. Successively, from each retina, light energy will be converted into electrical energy and consequent nerve impulses so that can be analyzed and interpreted by the visual cortex. This mechanism is called the visual pathway (Figure 1). The visual pathway starts at the retina and finishes in the primary visual cortex (called also striate cortex, Brodmann area 17 or V1). Before describing accurately visual pathways, it is important to consider the mechanism whereby light enters through the pupil. The sphincter pupillae (contracts the pupil) and the dilator pupillae (dilates the pupil) adapt the size of the pupil in order to control the amount of luminous energy entering in the eye. The sphincter pupillae is controlled by the parasympathetic system and the dilator pupillae by the sympathetic system. The activation of these reflexes occurs by the proportion of light entering in the eye and reaching the retina. Successively, it follows the visual pathway until the optic chiasma and from there, passes on to the pretectal area of the midbrain activating the cranial nerves III (oculomotor) and the Edinger-Westphal nucleus. Both nerves allow the mechanisms of the direct and consensual pupillary light reflexes. On the other hand, mainly, the light penetrates all the layers of the retina to achieve the photoreceptor layer (formed by cones and rods photoreceptors). In this important layer starts the transduction phenomenon and the visual pathway. The impulses of the photoreceptors are mediated by the second afferent neuron, bipolar cells whose short axons terminate at the large ganglion cells (third neuron), partly interposed by amacrine cells (Wahlerluck et al., 1991). The axons of the optic nerve originate from the multipolar ganglion cells of the inner layer of the retina (third neuron of the visual pathway) and extend until the optic chiasma. The optic chiasma is located in the anteroinferior end of the hypothalamus. In the optic chiasma, fibers from the temporal hemiretina pass through the optic chiasma and, without crossing, continue through the optic tract on the ipsilateral side. Fibers from the nasal hemiretinas decussate in the optic chiasma and enter the optic tract of the opposite cerebral hemisphere (Carpente.Mb, 1965; Brown, 1967). The decussation in the optic chiasma represent an important contribution for the binocular vision. Specifically, axons from the temporal half of the left eye join decussated axons from the nasal half of the right eye to form the left optic tract. In opposite, axons from the temporal half of the right eye join decussated axons from the nasal half of the left eye to form the right optic tract. Then, the optic tracts follow the hypothalamus and curve to terminate in each lateral geniculate nucleus (right and left). Here, the majority of the crossed and uncrossed optics fibers fan out to form the optic radiations which course backwards and upwards to end in the primary visual cortex (V1) in the ipsilateral occipital lobe of the cerebral cortex where visual pathways terminate (Figure 1). In addition, axons from the right half of each eye project to the right occipital lobe and those from the left half of each eye project to the left occipital lobe. Due to the reversal of each retinal image, the left half of the visual field (left hemifield) is represented in the right cerebral hemisphere and the right hemifield is represented in the left hemisphere.



Based on Kahle W, Frotscher M: Color Atlas and Textbook of Human Anatomy, 5th ed. Stuttgart: Thieme. Vol. 3 p.355, 2003.

Figure 1. Visual pathways of the human visual system (Kahle W and Frotscher M, 2003).

Concerning receptive fields organizations, it is important to differentiate between retinal ganglion cells (including also geniculate cells) and cortical cells receptive fields. First of all, the organization of ganglion cells' receptive fields are constituted by the inputs of the photoreceptors cells (cones and rods). Each organization of ganglion cells is formed by a central and a surround region**.** These two regions reacted antagonistically to light. Two types of ganglion cells are present: "on-center" and "off-center". An "on-center" cell could be stimulated when the center is exposed to the light and conversely, inhibited when the light is presented to its surround region (Hubel and Wiesel, 1962). The off-center cell has the opposite effect compared to the "on-center" ganglion cells: stimulation in its surround region and inhibition in its central region (Figure 2).

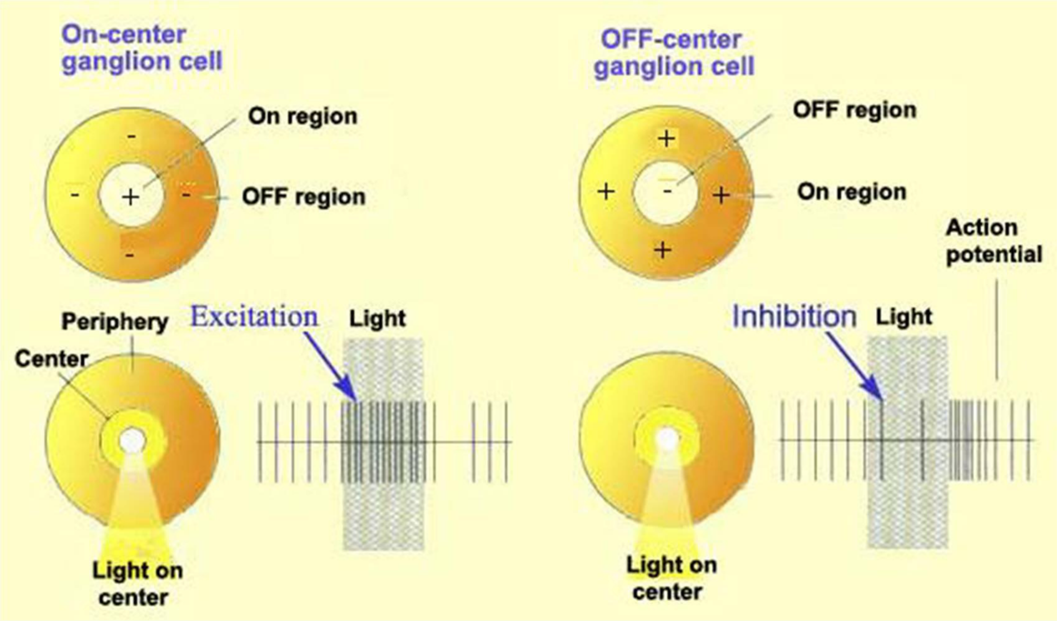


Figure 2. Illustration of the receptive field of the ON and OFF centers from retinal ganglion cells (Gao et al, 2008).

Regarding the cortical cells in the striate cortex, they also own their receptive fields which are divided into excitatory and inhibitory regions. Hubel and Wiesel classified in two groups: simple cells and complex cells (Hubel and Wiesel, 1962). Simple cells receptive fields arise from the convergence of geniculate receptive fields producing "on" and "off" subfields whereas complex cells arise from the convergence of the simple cells receptive fields which are formed by similar orientation but different positions (or spatial phases) generating "on" and "off" receptive fields responses (Ringach, 2004; Shi et al., 2019). As principal differences between these two types of cells, the simple cells could be monocular or binocular while complex cells are almost all binocular cells. In addition, the simple cells have "on" and "off" separated subregions whilst complex cells not. Thereafter**,** concerning the retinal ganglion and geniculate cells, they respond to a large spot of light covering the entire receptive field in contrast with the cortical cells react little or no to stimulation with large spots**.** The receptive fields play a preponderant role for the specificity of the stimuli, specifically, regarding its shape, its size and its orientation.

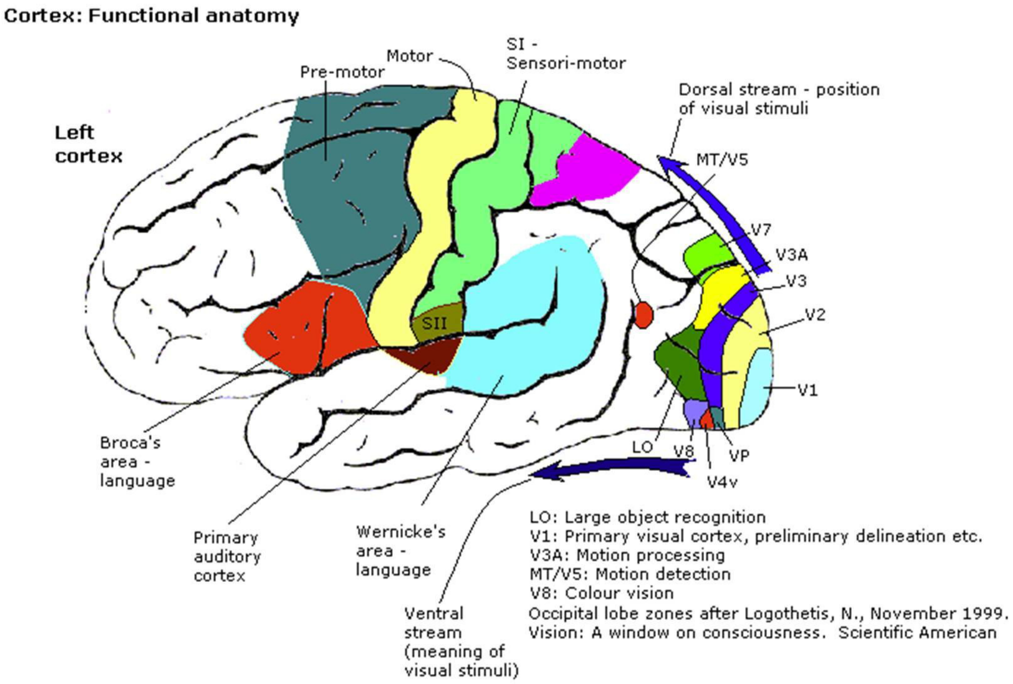


Figure 3. Functional anatomy of the cortex with the representations of the different visual areas, dorsal and ventral streams (Logothetis, 1999)

Depending on its position disparity, the two-complementary monocular receptive fields (right and left) would be identical in shape and slightly different in horizontal retinal position. In that respect, their neurons would require the sum of responses from two pairs of binocular simple cells, one with on-centers (excitatory) and the other with off-centers (inhibitory) to provide binocular visual threshold responses (Blakemore and Julesz, 1971; Blake and Wilson, 2011)**.** To achieve the strongest binocular response , it is necessary that the monocular stimuli could be optimal for the position offset or phase difference of the respective receptive fields (Blake and Wilson, 2011). Thereafter, the primary visual cortex is located on the medial surface of the occipital lobe and forms a complexly constructed cortical area (Wahlerluck et al., 1991). The visual information is firstly handed down on the primary visual cortex (V1) and successively, the visual information is transmitted to the extrastriate cortex. The extrastriate cortex is formed by different visual areas: V2, V3 and V4, which are subdivided in "where-information" and "what-information" processing areas (Felleman and Van Essen, 1991; Parker and Cumming, 2001) (Figure 3).

The dorsal stream allows to manage the "where-information" and the ventral stream handles the "what-information" pathway (Goodale and Milner, 1992; Milner, 1998). Goodale and Milner propose that the ventral stream of projections from the striate cortex to the inferotemporal cortex plays the major role in the perceptual identification of color, form and objects. On the other hand, the dorsal stream projecting from the striate cortex to the posterior parietal region mediates the required sensorimotor transformations for visually guided actions directed at such objects but also, interpreted spatial organization and spatial attention (Milner, 1998). In their study on human brain, Gulyás and Roland confirmed the importance of the dorsal and ventral visual streams in the stereopsis process (Gulyas and Roland, 1994) (Figure 3). Concerning the different visual areas, Hubel and Livingstone assessed with macaque neurophysiological and human psychophysics data that V2 is predominant in the binocular vision (Hubel and Livingstone, 1987). Thus, the stereopsis is represented not only in the dorsal streams areas including MT area (Hubel and Livingstone, 1987) but also in the ventral pathways (Parker, 2007). Concerning the depth perception, Preston et al using functional magnetic resonance imaging (fMRI), suggested that first and foremost, the dorsal stream processes the disparity content (disparity magnitude) followed secondly by categorical representations (disparity sign and depth position) in the ventral stream (Preston et al., 2008). So, both the dorsal and ventral streams are paramount in stereopsis and disparity processing (Parker, 2007; Blake and Wilson, 2011).

2.1.2. Binocular visual mechanisms: Binocular rivalry, disparity and stereopsis

Mainly, under natural conditions of binocular vision, each monocular dissimilar image is presented to corresponding regions of the retinas of both eyes, these can be fused to a single perceptual image succeeding stereopsis (Posner and Schlossman, 1951; Bishop and Henry, 1971; Bishop and Pettigrew, 1986) . For a correct binocular vision, each monocular eye matches with a normal retinal correspondence, namely, in case of normal retinal correspondence, both maculas must overlap and localize in the same point of the visual field and these points are called corresponding points. Specifically, when both eyes fix a determined point "F" (Figure 4), the two retinal images of the point "F" formed on the foveas ("FL" and "FR", left and right fovea, respectively) are seen singly (foveal binocular fixation). These two images corresponding to the retinal points of the left and the right eyes stimulating simultaneously, are called corresponding points. This is the theory of the corresponding points. From the corresponding points theory, the empirical horopter (Figure 4) represents the theoretical space where they are viewed singly when a subject fix binocularly a determined point of this space. As we can see in the Figure 4, a specific area called Panum's fusional area allows (if two retinal points are stimulated simultaneously) binocular single vision even if the two retinal points are not exactly projected onto the empirical horopter but slightly displaced compared to the fovea. This slight displacement respect to the fovea is called fixation disparity under normal binocular viewing conditions of the subject.

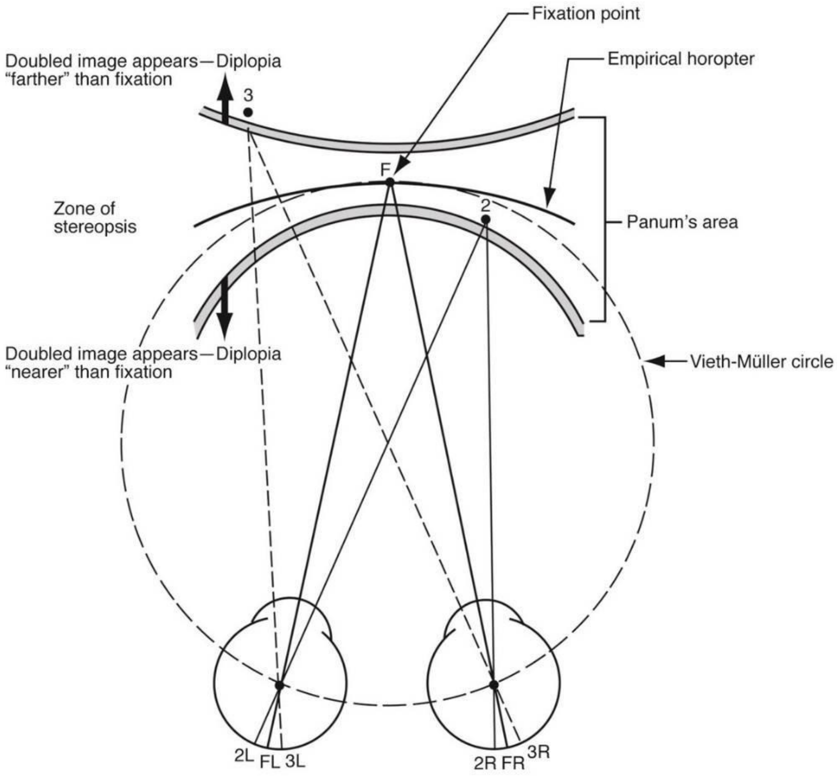


Figure 4. Empirical horopter (American Academy of Ophtalmology, 2015).

Thus, the two monocular images fuse in a single binocular image (second level of binocular vision) representing the cerebral integration of simultaneous monocular perceptions into a single binocular perception. This binocular mechanism can only occur until a limited extent determined by all the points situated within this Panum's fusional area. The retinal disparity initiates the stereopsis which is defined as the capacity and quality of the visual system to see in depth the surrounding environment. The stereopsis represents the highest level of the binocular vision (third level of binocular vision). As we said, the stimulus triggering the stereopsis is the disparity between the two monocular images. To explain the phenomenon of retinal disparity, we can specify respect to the Figure 4. In this figure, the point "2" is not on the horopter but onward situating onto the limit of the Panum's fusional area (zone of stereopsis) when the subject fix "F" (fixation point). The angle “2LFL" represents the eccentricity (or disparity) of "2” respect to "F" corresponding to the eccentricity of the left retinal image for "2" with respect to the fovea. Alike for the right eye, the angle “2RFR" corresponds to the eccentricity of the right retinal image for 2. The difference between the two angles formed on the retina of each eye is defined by Equation (1):

$$\eta = 2RFR - 2LFL \tag{1}$$

where "η" represents the disparity between the two points "2" and "F" and the point "2" is seen singly and stereoscopically. The disparity can be crossed if the object is onward respect to the empirical horopter and uncrossed if the object is backward respect to the horopter. To allow the stereopsis in binocular vision, several mechanisms must be taken into account. In 1959, Hubel and Wiesel (Nobel prize in Medicine in 1981) observed that each binocularly-activated cortical cell had two receptive fields, one for each eye, proving that the information from the two eyes merges earlier in the binocular visual mechanism (Hubel and Wiesel, 1959). In 1962, Hubel and Wiesel recognized that the neural pathways from the two eyes have to be sufficient different and dissimilar (disparity) to provide a neural mechanism for binocular depth perception (Hubel and Wiesel, 1962). Regarding the position disparity tuning curves of striate neurons, Bishop described the basis of the neural theory of binocular depth discrimination (Bishop, 1973). He insisted on the importance of vertical disparities. In fact, the cells of such vertical disparities are essential to provide the discrimination of horizontal stimulus disparities (Bishop, 1979). The presence of these disparities can arise as a result of natural eye misalignments (Bishop, 1979). Bishop theorized that vertical disparities are used to estimate absolute distance whereas horizontal disparities contribute to relative depth supported by psychophysics and neurophysiological evidence as the cortical cells discriminate also vertical and not only horizontal disparities (Bishop, 1979; Bishop and Pettigrew, 1986). An important understanding point in the stereoscopic perception and disparity was discovered by Julesz thanks to the use of the random-dot stereograms (Julesz, 1960). The specificity of these stereograms is given by a non-recognizable shape. Before these stereograms, it was assumed that the monocular recognition of form was preponderant and the first step in the stereoscopic perception. However, Julesz found that stereoscopic depth can be perceived without monocular and binocular cues except retinal image disparity. Therefore, the depth perception (with the influence of retinal disparity) plays the first role in the stereopsis neural mechanism followed by the recognition of form (Julesz, 1960) and, therefore, depth perception does not depends on the pattern recognition. Hubel and Wiesel supposed that not all the monocular cells are equally influenced by the two eyes suggesting that the different degrees of ocular dominance could provide the basis of the depth sensitivity mechanism. In the binocular visual system, sensory ocular dominance represents the condition where one eye is preferred to the other one for a perceptual visual task related to the sensory visual system (Porac and Coren, 1976).

Other important binocular mechanisms are represented by fusional processes. In a first step, it consists in the movement of the eyes fixing a determined object, which permit the reunification of the images. These movements are called fusional movements (Ogle et al., 1949). As stated before, the retinal disparity allows the fusion even if a tendency of the dissociation is present (heterophoria or phoria). It enables with the presence of fusional reserves in humans allowing when possible to correct and to keep retinal images in Panum's fusional area. Afterward, neural excitations of the two eyes arise and are transmitted to the visual cortex where information of the two eyes are unified (binocularity) and, consequently, the stereoscopic perception happens.

By contrast, in the Figure 4, the point "3" falls outside the empirical horopter and Panum's fusional area due to the raised disparity and consequently, non-corresponding points inhibiting a normal binocular vision and causing diplopia phenomenon. If the disparity is too large, the neurons in the brain cannot handle to create single vision and, as consequence, three phenomena could occur: binocular rivalry, monocular suppression or diplopia.

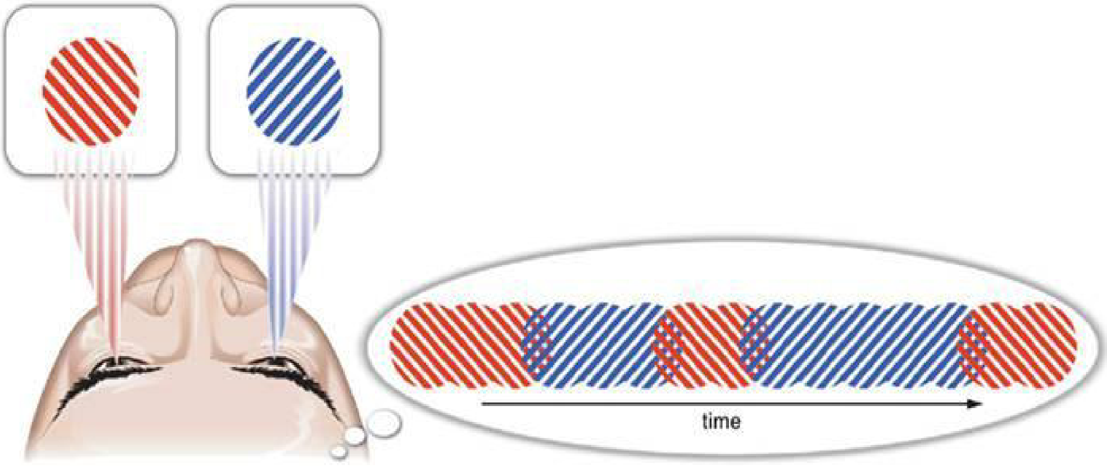


Figure 5. Binocular rivalry (Dieter and Tadin, 2011)

Firstly, the binocular rivalry is defined by the phenomenon where the two dissimilar images resulting from the two eyes compete for perceptual dominance in the primary visual cortex (Blake, 1989). In this situation, the image of one eye dominates when the image of the other eye is suppressed alternating the dominance perception regularly between the two eyes (Polonsky et al., 2000). This phenomenon is called eye-based rivalry (or conventional binocular rivalry). As observed in the Figure 5, the red and blue gratings, showed to the left and right eye, respectively, cause binocular rivalry and dominance perception in the visual perception. Sometimes the visual cortex would interpret the red grating, sometimes the blue one but also, sometimes a mix between both gratings. These alternating periods for the dominant eye continually change taking in consideration a few fleeting moments of mixed perception. In addition, in binocular rivalry, the visual perception seems to be dominated by extended periods of one or the other orientation, with the two eyes alternating in conscious perception slowly and stochastically (Logothetis et al., 1996). This visual perception varies in strength due to main factors like the contrast or the type of the stimulus changes (Logothetis et al., 1996). Logothetis et al also concluded that during binocular rivalry, it is the stimulus (stimulus rivalry) and not the eye (eye-based rivalry) that plays an important role. However, Lee and Blake specified that the stimulus rivalry is strictly restricted to a range of spatial and temporal frequencies compared to conventional binocular rivalry (Lee and Blake, 1999). Another distinction between stimulus and conventional rivalry is in their dependence on stimulus size and contrast (Bonneh et al., 2001). Thereby, the binocular vision is disrupted when binocular rivalry occurs. The stereopsis in the presence of rivalry depends on the contrast of the two-half images. It could be superior when contrast levels are low but rivalry could dominate when contrast is high (Blake et al., 1991). Also, degradation in stereopsis appears when the two half-images have reverse contrast half-images and the stereopsis is completely removed in case of these two half-images having reverse contrast are represented by random-dot stereograms (Cogan et al., 1995). Then, dissimilar spatial frequency and orientation between the two-half images could undermine the quality of the stereopsis (Buckthought and Wilson, 2007). In binocular rivalry, the subject is unable to control and choose an individual image. It is an unconscious and neural phenomenon. Measuring with functional magnetic resonance imaging (fMRI), Polonsky et al investigated fMRI signals in early visual cortex while subjects viewed rival dichoptic images of two different contrasts: in the non-dominant eye, the stimuli was represented by lower contrast and vertical-red sinusoidal gratings while in the dominant eye, the stimuli was represented by higher contrast and horizontal-green sinusoidal gratings (Polonsky et al., 2000). They observed that the activity in primary visual cortex (V1) increased when subjects perceived the higher contrast pattern and decreased when subjects perceived the lower contrast pattern. The V1 activity were equivalent to other visual areas (V2, V3, V3a and V4) suggesting that the neuronal mechanisms responsible for binocular rivalry occur primarily in later visual areas (Polonsky et al., 2000).

Secondly, monocular suppression (or monocular deprivation) represents the phenomenon where one eye is suppressed by the visual system. In the situation where the left and right foveal images do not correspond, the brain can temporarily suppress one of the two different images removing in this way the interocular conflict. This mechanism is called rivalry suppression and it could involves alternations in dominance between the two eyes (Blake, 1989). Another mechanism called chronic suppression causes the monocular suppression which can be used in some individuals as an adaptive response to avoid diplopia or visual confusion due to eye misalignment (Blake, 1989). In the chronic suppression, these persons suppress foveal vision in one eye under natural viewing conditions. Some individuals are able to control which eye is suppressed. Normally, in this situation, the person alternates one eye for near vision and the other one for far vision. This mechanism is called alternating suppression. Historically, Wiesel and Hubel showed that the deprivation in one of the kitten eyes caused the deactivation of visual cortical neurons (Hubel and Wiesel, 1962). Two main reasons could explain this disabling condition. First, the monocular suppression reduces its afferent cortical terminations and second, it would appear that some contributions are still conserved but, they are suppressed by inhibitory influences from the normal eye (Movshon, 1981).

Specific zones of suppression are localized in the visual system highlighting the cortical representation of the two retinae. The sizes of these zones are smaller in the fovea region and increase progressively with the retinal eccentricity (Blake et al., 1988). In addition, Hubel and Wiesel theorized the concept of hypercolumn defined as a group of cortical cells which provide a complete representation of orientations for both eyes (Hubel and Wiesel, 1962). Each hypercolumn is constituted by ocular dominance columns and orientation columns representing a targeted region in the visual field (Hubel and Wiesel, 1962). A hypercolumn covers the same area of cortex and analyzes a section of retina whose area is related to its specific receptive field and its constituent neurons (Blake, 1989). In this context, several authors assumed that a suppression zone could be formed by the entirety receptive field sizes of neurons representing a hypercolumn in the visual cortex (Hubel et al., 1978; Koenderink and Vandoorn, 1987).

Moreover, the strength of inhibition causing monocular suppression is dependent of the magnitude of monocular neurons innervated by the suppressed eye and the duration of the monocular deprivation is due to the strength of excitation generated by the suppressed stimulus (Blake, 1989). A strong monocular stimulus would generate potent inhibition and a weak monocular stimulus would cause a weak inhibitory signal (Blake, 1989). To assess the strength of inhibition, Holopigian et al investigated the relation between the depth of suppression (defined as the amount by which the monocular contrast increment threshold for an eye was elevated by stimulation in the contralateral eye) and the degree of amblyopia (defined as the difference in monocular contrast thresholds between the two eyes) in normal and amblyopic subjects. They found a significant negative correlation between depth of suppression and degree of amblyopia showing that observers with amblyopia presented weaker or no suppression. They highlighted that this negative correlation was revealed when the two eyes viewed orthogonally oriented contours. They concluded that when an eye is amblyopic, there is no longer a need for strong suppression of that eye by the contralateral eye (Holopigian et al., 1988). Also, they found that the higher the interocular difference in visual acuity, the higher threshold in the monocular suppression (eye with the lowest visual acuity). Recently, Marella et al found in subjects with unilateral and bilateral keratoconus that the eye with lesser disease severity dominated binocular viewing whereas the eye with poorer vision was suppressed. This monocular suppression depended on the extent of the bilateral disease severity, optical correction and the target spatial frequency (Marella et al., 2021).

Finally, as we stated previously before, if the disparity is too large, the neurons in the brain are not able to maintain single vision. In circumstances where neither binocular rivalry nor monocular suppression is established, diplopia occurs. Diplopia is defined as the impossibility to fuse binocularly a single image of an object. Under these conditions, the subject will perceive two images (one for each eye) of a single object. Diplopia can be: intermittent or permanent, monocular or binocular and from different directions (horizontal, vertical or oblique). It is important to specify that diplopia can appear merely in one eye. One eye can perceive two images of a single object even if the unaffected eye is covered (Fincham, 1963). This category of diplopia is called monocular diplopia. In monocular diplopia, the two images are similar in size, without distortion and almost superimposed (Fincham, 1963; Records, 1980). Usually, the two images in physiologic monocular diplopia are similar in size without distortion and nearly superimposed: one image named primary image will be detected bright and clear whereas the other one (the secondary image) will be seen less clear (Records, 1980). Monocular diplopia is always acquired physiologically (like uncorrected refractive errors, astigmatism) or pathologically (cataract, corneal disease, primary and secondary visual cortex disorder, macular disease…) but never congenital (Records, 1980; Bartiss, 2018). Monocular diplopia can be resolve with the use of a pinhole (Phillips, 2007). On the other hand, binocular diplopia happens suddenly and binocularly. Several causes are responsible of this diplopia: iatrogenic reasons due to ophthalmic surgical procedures (cataract surgery), neurophtalmologic reasons and strabismus (Bartiss, 2018). For instance, once the fusional reserves do not achieve to maintain correspondence of the visual objects on the retinas of the two eyes (misalignment of the visual axes), a breakdown in the binocular system is involved causing diplopia when the two eyes are viewing simultaneously. This diplopia disappears occluding either eye. For example, convergence insufficiency is the most common cause of horizontal binocular diplopia at near which induce exophoria or even exotropia. This binocular diplopia can be treated with fusional vergence exercises or the anteposition of a prism (Tamhankar et al., 2012). Another common cause of binocular diplopia could be induced by refractive error like displacement of optical centers on prescription spectacle lenses. This displacement produces a prismatic effect. In addition, anisometropia superior to 1.5 D could lead to diplopia resulting in image size difference between the two eyes (aniseikonia) which could be corrected with contact lenses (Phillips, 2007). Furthermore, ocular motor palsy represents an important cause of diplopia in the elderly people due to monovascular ischemia to one of the ocular motor nerve (third, fourth or sixth cranial nerves) being the third nerve palsy the most common provoking strabismus and hence, diplopia. Binocular diplopia can be also due to: Parkinson’s disease, cerebral vascular accident or neurologic conditions (myasthenia gravis). To conclude the diplopia phenomenon, physiological diplopia is a normal phenomenon and can appear in patients without neurological consequence. It is possible to highlight fixing a far object (for example the fixation point F in the Figure 4). Unconsciously, the others points in the visual field placed forward or backward the fixation point could be perceived double. In the Figure 4, fixing the fixation point F, a forward point respect to this point will be perceived in diplopia (diplopia "nearer" than fixation) and a backward point respect to this point will be seen in diplopia "farther" than fixation.

2.2. GENERAL ASPECTS IN INTEROCULAR DIFFERENCES AND BINOCULAR SUMMATION

2.2.1. Interocular differences

Interocular differences are defined as the differences between the two monocular eyes concerning a determined visual parameter which could be induced, for instance, by the difference in intraocular scattering, optical quality (which can be difference in ocular aberrations), corneal asphericity, refraction, pupil size…

A theory from Li et al suggested a specific organization in vision. In this theory, the retinal images of the two eyes are processed by two binocular channels. The first, called B+ (binocular summing), handles to sum the signals of the two eyes while the second one (called B- or binocular differencing) is dedicated to discriminate the two signals originating from the two eyes, in such a way they constitute an important and efficient code for the binocular information (Li and Atick, 1994). These channels are involved in several visual tasks such as contrast detection, motion perception, orientation processing, binocular rivalry and stereopsis. To support this theory and understand the different contributions between the two channels (B+ and B-), Kingdom et al conducted two experiments to identify the detection mechanisms on interocular differences using luminance contrast (Kingdom et al., 2019). The test patterns used were multi-spatial-frequency luminance-grating which were oriented horizontally. They may vary the amounts of interocular difference in grating phase, resulting in varying degrees of local interocular contrast difference. In their first experiment, the participants had to discriminate between a test pattern with an interocular difference upward from zero (binocularly correlated) and the other one, with a larger amount of interocular difference. In the second experiment, the participants had to discriminate between a test model with an interocular difference that ranged downward from a maximum (binocularly anticorrelated) and the other one with smaller interocular difference. This study concluded that the first experiment could be mediated by the binocular differencing channel (B-) whereas the second experiment could be determined by the binocular summing channel (B+). Binocular summing channel seems to be inhibited when signals from the monocular channels are stronger due to a larger amount of interocular difference (Kingdom et al., 2019).

It is important to specify that several factors influence interocular differences. Firstly, different refractive errors between the two eyes can cause anisometropia and they are largely widespread along the population. It is well known that if the interocular differences in refraction are strong between the two eyes, amblyopia could be acquired (Donahue, 2006). A common example, where interocular differences in refraction are induced, is in "monovision" technique for the presbyopia correction. In this technique, one eye is corrected for distance and the other for near inducing important interocular differences between the two eyes. Normally, due to the elevate amount of blur, one image is suppressed depending on where the subject view: if the subject fixes an object at far, the eye with near correction is suppressed and vice versa. Kompaniez et al investigated the effect of blur adaptation using two methods. One called *monocular adaptation* which consisted in the presentation of an adapting image to one eye and a uniform field to the other eye. This condition was employed to determine the degree of interocular transfer comparing the strength of adaptation in the two eyes. The second method called *contingent adaptation* assessed the blur adaptation showing monocularly a single adapting image (the two eyes saw the same scene) but with a different level of blur between the two eyes. The adaptation to differences in blur was arisen by differences in refractive errors between the two eyes. They suggested that the aftereffects depend strongly on the sharper image between the two eyes and that the binocular adaptation to blur is also biased by the sharper of the two eyes' retinal images (Kompaniez et al., 2013).

Secondly, an important factor to take into account in vision assessment is age (Ross et al., 1985; Pardhan, 1996) . This aspect could also influence on interocular differences. Wood and Bullimore found that in the assessment of low contrast visual acuity, interocular differences are considerably influenced by age (Wood and Bullimore, 1996).

Thirdly, interocular differences in luminance or contrast between retinal images modify perception causing interocular delays: the speed of visual processing for low-spatial-frequency information is faster than that for its high-spatial-frequency (Diamond, 1958; Kitaoka and Ashida, 2007). Hyun Min et al investigated the visual perception when visual targets moving in fronto-parallel motion are presented to the eyes. In this circumstance, lower luminance or contrast delays the speed of visual processing. In their study, they also contributed through an accurate paradigm based on the Pulfrich effect (stereo-motion phenomenon creating the illusion of depth) to consider how spatial frequency and size could influence the speed of visual processing. They found that interocular spatial frequency differences, but not interocular size differences of image features, produce interocular processing delays (Min et al., 2020). Similarly, Reynaud and Hess showed psychophysically that interocular contrast differences resulted in an illusory percept of motion in-depth. They explained this phenomenon arguing that difference in contrast and also luminance modified the mechanisms of visual neurons producing interocular processing delays (Reynaud and Hess, 2017). Consequently, interocular differences in luminance affect several visual parameters: visual acuity, contrast sensitivity, stereoacuity, fusion, retinal image quality, higher-order aberrations… Several studies handled interocular differences in these visual parameters taking into account their impact on binocular vision, visual tasks or clinical implications. Kirschen et al investigated interocular differences in visual acuity and stereoacuity in two presbyopic soft contact lenses using monovision technique to correct presbyopia (Acuvue Bifocal and Surevue). In this study, the contact lens that showed less interocular acuity difference showed an improved stereoacuity, decreasing suppression (caused by monovision) between near and far (Kirschen et al., 1999). Thompson et al suggested the strong relationship between interocular differences in visual acuity and the magnitude of anisometropic ametropia (Thompson et al., 1996): the higher the differences in visual acuity, the higher the degree of anisometropia. So et al also investigated interocular acuity differences and the effect of monocular blurring on stereopsis. They concluded that interocular acuity differences altered negatively stereopsis such as occurs in the deficits of fine stereopsis in case of anisometropic amblyopia (So et al., 2014).

On the other hand, Schor and Heckmann inquired into interocular differences in contrast and spatial frequency on stereopsis and fusion. They found that reduction in stereoacuity due to interocular difference in contrast was lower for higher spatial frequency. For the low spatial frequencies, the stereothreshold was higher when reducing the contrast of one image compared to equal contrast reductions of both images. Regarding vertical and horizontal fusion, horizontal fusion was reduced more than vertical fusion for interocular contrast differences especially at higher spatial frequencies (Schor and Heckmann, 1989). Other authors studied the influence of the interocular difference on binocular contrast sensitivity in amblyopia (anisometropic amblyopes and strabismic amblyopes) finding that increases in these interocular differences produced binocular inhibition at high spatial frequencies (Pardhan and Gilchrist, 1992).

In addition, several studies attested deterioration in stereopsis respect to interocular differences in retinal image quality. Castro et al found that the higher the interocular differences, the higher the deterioration in stereopsis. They confirmed the decrease in binocular visual performance through the increase of these interocular differences (Castro et al., 2009). Similarly, Castro et al correlated the influence of interocular differences in optical quality and maximum disparity: the lower interocular differences, the higher maximum disparity (Castro et al., 2010). In another study, they confirmed the deterioration of the range of stereoscopic perception with interocular differences in optical quality adding that a greater perception of halos in these conditions occurs (Castro et al., 2017).

Interocular differences in higher-order aberrations also impacted negatively binocular visual performance. Jimenez et al proved that the stereopsis declined with the rise of interocular differences in higher-order aberrations (total, coma, and spherical aberration) affecting binocular vision (Jimenez et al., 2007). In other work, Jimenez et al found a decline in the upper disparity limit after LASIK surgery. They highlighted that this deterioration was significantly correlated with an increase in the postsurgical interocular differences in higher-order aberrations, corneal asphericity, and presurgical anisometropia (Jimenez et al., 2008a).

Finally, pattern visual evoked potentials (PVEP) and pattern electroretinograms (PERG) allowed investigating interocular differences in visual latency and amplitude. In a first research, Plainis et al measured interocular differences in visual latency and amplitude for PVEP induced by small-aperture contact lens designed for presbyopes. In their research, the small aperture wearing on the non-dominant eye reduced the amplitude of the PVEP and increased its latency (Plainis et al., 2013b). The anisocoria induced by the consequent use of small aperture in one eye provoked interocular differences in retinal illuminance on the subjects. This caused increases in visual latency comparing to others studies where neutral filters were used to induce illuminance differences (Heron et al., 2002). These differences in latency could result in distortions in the perception as positions or movement of the objects due to the Pulfrich effect (Plainis et al., 2013b). In a second study, Fejes et al also investigated whether amplitudes and latencies in PERG and PVEP corresponded in lateral dominance or in similarities on eye-side contributions. They found interocular differences recording PERG and PVEP in 77 normal subjects disclosing the importance to take into consideration difference between the two eyes in order to avoid misinterpretation in pathological diagnostics (Fejes et al., 2014).

2.2.2. Binocular summation

Binocular summation (BS) represents a visual phenomenon, which occurs with the unification of both monocular perceptions in a single one. Indeed, both corresponding monocular similar images fuse. Its monocular signals are processed by cortical and neural mechanisms which converge in the cerebrum resulting in a higher binocular signal (Eysteinsson et al., 1993). Binocular summation specifies the performance of binocular visual perception compared to the best monocular one in a determined psychophysical experiment (Blake and Fox, 1973). A ratio is normally defined to assess the binocular (B) performance respect to the best monocular one (M) for a specific visual function. Even if, in some visual measurements such as the amplitude of visual evoked potential, the mean monocular value is calculated to compare to the binocular one in binocular summation ratio (Apkarian et al., 1981; Leguire et al., 1991). In this regard, different degrees of binocular interaction are defined according to the value of the corresponding binocular summation calculated (Blake and Fox, 1973; Apkarian et al., 1981):

- BS < 1 (B < M): ***Inhibition*** of the binocular system. the amplitude of the binocular performance is less than the monocular one. Inhibition in the binocular summation could occur for unstable binocular vision.
- BS =1 (B = M): ***Zero binocular summation***. The binocular response is equal to the monocular one.
- 1 < BS < 2 (M < B < 2M): ***Partial summation***. The binocular performance is better than the mean monocular one. Independence between the two eyes responses could arise assuming for example, saturation in the binocular system or the presence of different levels of interaction between the monocular and binocular mechanisms.
- BS = 2 (B = 2M): ***Summation or linear summation.*** The binocular response is exactly the sum of the two monocular responses in case of independence between them.
- BS > 2 (B > 2M): ***Facilitation.*** The binocular response is superior to the sum of the two monocular responses. Taking into this consideration, this supposed the presence of a neural stereoscopic depth mechanism.

So, the binocular summation values could depend on the interaction between the two monocular systems. Two patterns were elaborated to explain the mechanism of the binocular summation: probability summation and neural summation.

Pirenne (Pirenne, 1943) hypothesized that the binocular detection should equal the monocular probability detection of a lighting flash of twice the luminance (the sum of the two monocular luminances). But, contrary to its expectations, its results found that the double-luminance monocular condition was higher than the provided in the binocular probability theory suggesting consequently, that only the probability summation is not sufficient to explain the higher interaction of the two eyes. The probability summation model is defined as the improvement in binocular performance is merely obtained by the simultaneous presentation of the two monocular providing two opportunities to detect the corresponding output. So, statistically, the additional opportunity could allow to enhance the detection of the stimulus (Blake and Fox, 1973). In other terms, the relative superiority of binocular viewing is superior to the planned by the probability summation theory (Blake and Fox, 1973; Blake et al., 1981; Blake, 1989). It was considered that some neural interactions were present to explain improved results than expected. So, the hypothesis about these interactions explaining better findings in binocular vision defines the basis of the neural summation theory. In consequence, as mentioned above with the neural summation theory and the consequent superiority of the binocular summation, this could give an explanation about the presence of binocular neurons in the integration of the binocular information specifying that the underlying binocular neural interaction could be excitatory, not inhibitory (Blake, 1989). In case of dissimilar monocular stimuli, the detectability of a monocular specific target declines compared to the situation of two identical monocular targets. In this condition, binocular rivalry occurs and hence, the binocular summation decreases respect to a non-rivalry conditions (Westendorf et al., 1982). In that respect, the sensitivity of the suppressed eye is reduced against the dominant eye. Nevertheless, the remaining sensitivity of the suppressed eye is integrated to the dominant eye and binocular summation happens even if it is inferior with regard to the non-rivalry conditions (Westendorf et al., 1982). According to Westendorf et al and the binocular summation theory, binocular neurons are responsible for the neural summation while monocular neurons involve the probability summation. So, during rivalry, the monocular part diminishes due to the suppressed eye sensitivity causing lesser contribution from the probability summation respect to the neural one.

Binocular summation depends on several optical factors that could influence this visual phenomenon and, successively, binocular visual performance. It is discussed as follows in accordance with the classification performed by Blake and Fox (Blake and Fox, 1973).

- *Individual differences.* It is well-known that humans do not possess the same ocular characteristics (for instance, the degree of ocular dominance). Concerning a determined visual task, it clearly assumes that each participant could obtain different results. As stated before, to ease binocular summation, it is important to achieve similar monocular sensitivity. In case of binocular rivalry, the more sensitive eye could dominate during the binocular viewing. Then, the binocular summation value could differ respect to the degree of monocular sensitivity. It is not mandatory that binocular summation occurs in the entire population and a part could suffer difficulties in binocular mechanism due to ocular pathologies (Castro et al., 2011; Olson et al., 2017), ocular disorders as amblyopia (Holmes and Clarke, 2006), interocular differences after refractive surgery (Anera et al., 2011) or even stereoblind (Lema and Blake, 1977). So, the efficiency of binocular viewing varies by person.

- *Pupil size.* The amount of light entering the eye is proportional to the square of the pupil diameter. As it is well established, during binocular viewing, the light entering each monocular pupil size is smaller than the light reaching during monocular viewing. For instance, in threshold experiment, it is necessary to have the same amount of light when we want to compare monocular and binocular measurements. This pupil size difference can perturb the correct assessment of the binocular summation. Particularly, during monocular viewing, in the case of larger pupils, the monocular threshold obtained could be lower compared to the binocular one influencing the binocular visual performance (Blake and Fox, 1973). Binocular summation could be affected by cortical pupil mechanisms. Medina et al studied the effect of pupil size on binocular summation at suprathreshold conditions. Visual reaction times (VRT) were chosen as an indicator for the binocular summation at suprathreshold levels. They found that visual reaction times (VRT) for natural pupils were lower than artificial pupils concluding that pupil size influenced binocular summation for suprathreshold conditions (Medina et al., 2003). Castro et al simulated corneal-inlay implantations through different pupil sizes (4mm, 3mm and 2 mm placed in dominant and no dominant eye inducing anisocoria in healthy young subjects. They stated for all the simulated conditions that binocular summation (in contrast sensitivity and visual disturbance index) diminished strongly respect to the natural pupil condition. In most of these simulated situations, binocular summations were inhibited at least for one of the two binocular summations calculated (contrast sensitivity and/or visual disturbance index) (Castro et al., 2016) .

- *Fixation.* During binocular viewing, the monocular fixation of both eyes allows to slightly improve the monocular performance beside monocular viewing achieved occluding one of the two eyes. In this sense, Collier et al (Collier, 1954) found that binocular threshold was always higher than monocular one in monocular fixation conditions. As explanation, Collier et al indicated that the cause could be the stimulation of non-corresponding retinal points of the unfixed eye.

- *Visual task characteristic.* Binocular summation could depend on the visual task involved: detection, discrimination, recognition or resolution. Campbell and Green measured monocular and binocular thresholds for different contrast grating detection varying the luminance. Taking account these considerations, they obtained that binocular sensitivity was higher than the monocular one for a constant value of $\sqrt{2}$ resulting in lower binocular thresholds. They argued that this value was the sum of the two eyes and the addition of a noise independent of these eyes concluding that neural summation is responsible of this higher value (Campbell and Green, 1965b). Home studied different type of visual tasks including contrast detection, spatial resolution task (visual acuity) and contrast sensitivity for a recognition task with different levels of luminance. He found similar binocular performance value (recognition task and detection experiment) that Campbell and Green in contrast sensitivity (BS=1.42). However, he found that a value of 1.5 for the BS would be more accurate regarding a contrast detection task (assuming monocular viewing with the dominant eye) and even 1.6 in the case of the monocular viewing involves the non-preferred eye). Its results concluded that binocular summation is reduced in visual tasks where the accommodative-vergence cues are weak (Home, 1978). The complexity of the visual task plays an important role in the cortical visual processing and the subsequent lower value in the binocular summation (Frisen and Lindblom, 1988). For example, they identified that the detection task obtained higher values in summation respect to the resolution task. So, in the threshold visual tasks such as increment detection, form recognition or spatial resolution task, binocular performance seems to be greater than that predicted by probability summation paradigm being neural interaction a paramount parameter in the binocular summation (Blake et al., 1981).

- *Age*. On the other hand, an important factor in binocular performance is represented by age. Age has been investigated on many visual functions to understand the impact and the influence of this factor on vision. It is well known the different ocular structures and the consequent retinal image quality impair with age disclosing several ocular pathologies as cataract (Vilaseca et al., 2012a) or age-related macular degeneration (Ortiz et al., 2010). In that respect, age affects also the binocular performance. Pardhan compared the binocular summation in young and older healthy patients. She measured the binocular and monocular contrast sensitivities at two spatial frequencies (1 and 6 cpd) for these two categories revealing a significant reduction in binocular summation with age (Pardhan, 1996). The reasons proposed by Pardhan was the loss of cortical cell and the increase of monocular sensitivity differences with age.

- *Interocular differences*. Interocular differences take an important part on binocular performance, as summarized in subsection 2.2.1. Several studies highlighted that increases in interocular differences affected negatively the binocular summation and consequently, binocular visual performance. For instance, in healthy young subjects, Pardhan and Gilchrist found deterioration in binocular summation proportional to the increase of interocular differences in optical quality (defocus) (Pardhan and Gilchrist, 1990). In addition, Jimenez et al disclosed that differences in corneal asphericity influenced binocular summation decreasing the binocular contrast-sensitivity function

(Jimenez et al., 2003). Similarly, Castro et al showed that increases in interocular differences in retinal image quality parameters yielded contrast binocular summation reduction (Castro et al., 2009). Increases in Interocular differences in higher-order aberrations as spherical aberration, coma and total aberration impaired binocular summation (contrast sensitivity) (Jimenez et al., 2008b). Castro et al induced interocular differences in optical quality by anisocoria and defocus causing decreases in binocular summation when the interocular differences increases (Castro et al., 2016). Subsequently, differences between binocular and monocular measurements have been taken in consideration in order to quantify binocular summation for different visual functions.

- *Luminance.* Contrast sensitivity measure has been used to calculate binocular summation for contrast threshold. Specifically, absolute threshold was inquired to assess this summation. Absolute threshold refers to a detection of a small spot of light (in fovea or periphery) presented against a dark background. In these measurements, the minimum luminance and duration for detection of this stimulus is determined. Neural and perceptual responses at specific visual stimuli depend on this luminance. Indeed, low luminance levels decrease the spatial and temporal contrast sensitivity function and the visual responses (Swanson et al., 1987). Specifically, in case of luminance reduction in only one eye, this hinders the correct binocular viewing inducing a deterioration in binocular summation (Baker et al., 2007b). Baker et al found that reduction of one eye's luminance induced by neutral density filters in normal observers affected negatively the binocular measurements inhibiting its contrast binocular summation. Leonards and Sireteanu found that, in normal observers, progressive reduction of one eye's stimulus luminance with neutral density filters produced time courses similar to those of amblyopic subjects and caused diminution in the binocular perception (Leonards and Sireteanu, 1993). Richard et al measured binocular summation in contrast detection thresholds with and without neutral density filters placed on one eye. Without filter placed, they found linear binocular summation (BS=2). They disclosed that binocular summation ratios in contrast sensitivity decreased as a function of filter density (lower luminance), but always remained superior to the unfiltered eye value. In other words, binocular summation ratios were superior to 1 indicating partial summation in all the luminance levels. They suggested that a dichoptic decrement in luminance could only impact the neural responses of the filtered eye while binocular neural responses diminished slightly (amplitude) (Richard et al., 2018). Schwarz et al studied the effect of different levels of luminance (0.2, 0.02 and 0.002 cd/m^2) through different neutral filters placed on the eyes (monocularly and binocularly) on binocular summation for contrast sensitivity. They corrected monocular ocular aberrations through the use of adaptive optics. They highlighted that binocular performance in contrast increasing significantly with the luminance reductions after correcting ocular aberrations monocularly with adaptive optics (Schwarz et al., 2014).

- *Brightness.* Binocular brightness summation is defined as the ratio between binocular and monocular brightness of suprathreshold stimuli (Blake and Fox, 1973). To assess this summation, a simple experiment can be performed. A subject fixes a determined object binocularly and then monocularly occluding one eye. This subject will not observe in binocular viewing neither doubling of brightness nor increases in brightness. Blake and Fox suggested that maybe a slightly increment could be detect in brightness in sensitive experiments. It is important to specify that binocular brightness summation is a subject of disagreement and a lack of studies are reported (Blake and Fox, 1973). Some authors (Leibowitz and Walker, 1956) found that, under binocular viewing conditions, a suprathreshold stimulus is viewed brighter compared to monocular one. Engel et al contradicted this finding arguing that the results were contaminated by lateral interactions between test and the comparison targets (Engel, 1967). A controversy was also discussed about the metric expressed: luminance, brightness or discrimination responses. On the other hand, another experiment can be achieved. A subject fix binocularly a specific object at a determined distance with the two eyes unequally illuminated placing a neutral filter in one of the two eyes. Under these conditions, binocular brightness impression (binocular viewing) would be inferior to the brightness value of the unfiltered eye (monocular viewing). In fact, reducing the visual stimulation and occluding the filtered eye, a paradoxical increase in brightness is revealed in the unfiltered eye. This phenomenon was first described by Fechner (1860) and it is called Fechner's paradox. An explanation could be that in these specific brightness conditions, binocular brightness is the average of the two-monocular brightness (filtered and unfiltered eye).

- *Reaction time (RT).* Mainly, binocular summation is provided by threshold measures of sensitivity in different conditions as low contrast or intensity or short time presentation of the stimulus. Even if this approach is very useful in the binocular visual performance, a limitation is given by suprathreshold conditions measurement such as implied in daily visual environment. To solve this issue, studies investigated visual reaction time of a clear stimulus. For normal healthy observers and a wide range of contrast sensitivity values, they found that binocular reaction time was faster than monocular ones even at high spatial frequencies and its binocular summation was greater than probability summation expected being higher than 40% (Blake et al., 1980). In this study, patients with deficient stereopsis performed binocular summation but lower than subjects with normal stereopsis.

- *Ocular aberrations.* The interocular differences in ocular aberrations could influence negatively binocular summation ratio and consequently, binocular visual performance (Jimenez et al., 2007). To this end, other studies investigated how the correction of the higher-order aberrations could influence binocular summation. For this purpose, Schwarz et al (Schwarz et al., 2014) corrected higher-order aberrations (HOA) using a Hartmann-Shack sensor. They compared the effect of the corrected HOA on binocular simulation and under different luminance levels. Under high luminance, binocular summation ratios (contrast) with or without HOA correction were equal (BS = 1.16). Contrariwise, under low luminance, the HOA correction increased significantly binocular summation compared to uncorrected HOA (1.30). In other research, Sabesan et al performed the correction of HOA using a binocular adaptive optics device. They found that binocular performance was improved in contrast sensitivity and visual acuity correcting ocular aberrations compared to uncorrected aberrations condition, but binocular summation was the highest when aberrations were uncorrected. They suggested that binocular visual system implemented a compensatory effect to reduce optical blur caused by higher-order aberrations (Sabesan et al., 2012b).

- *Electrophysiology.* In their study on amplitude and latency in suprathreshold responses of the pattern reversal visual evoked potentials (PVEP), Plainis et al found in healthy young subjects that binocular summation ratio in P100 amplitude and latency were correlated linearly with the amount of defocus: the higher the amount of defocus, the higher the binocular summation. They suggested that increased retinal blur attenuated image contrast and an overall loss in its modulation transfer function. They argued that increments in binocular summation with retinal blur might be the results of the activation of a larger population of binocular neurons at close-to-threshold (Plainis et al., 2011). Czainska et al highlighted in healthy young subjects, partial binocular summation (between 1.2 and 1.7) in all the components (amplitude and latency) of early and late visual evoked potentials named N75, P100 and N145 being the highest value in the N75 amplitude showing better binocular visual performance than monocular one (taking into account the dominant eye). Binocular increments in visual evoked potentials could be obtained by reduction in the noisy neural representation (Czainska et al., 2018).

- *Visual Acuity.* Visual acuity involves spatial resolution task. According to the optotype (Snellen letters, Landolt C, ETDRS chart), binocular summation ratio for this visual function could be influenced. Another important factor to take into account is the low or high contrast applied in the visual acuity measurements. In the main viewing conditions, binocular summation is positive proving the superiority of the binocular system concerning visual acuity measurement. In healthy young subjects, binocular summation ratio in visual acuity ranged between 1.05 and 1.11 for high contrast levels (Campbell and Green, 1965a; Cagenello et al., 1993;). Sabesan et al confirmed positive binocular summation of a value of 1.05 in healthy young subjects measured with Snellen letters (Sabesan et al., 2012b). Heravian et al found an improvement on binocular visual acuity of 11.3% measured with the Landolt C optotype. Therefore, a mutual agreement exists in relation with the increment of the binocular visual acuity in a healthy group. Nevertheless, in a complex recognition task as Vernier acuity (hyperacuity), a lack of agreement about binocular summation efficiency is present. Banton et al (Banton and Levi, 1991) investigated a large range of contrasts from the line-detection threshold, to approximately 20 times threshold. They found better results under binocular viewing than monocular in all the contrasts used, although at higher contrasts, the binocular advantage decreased due to saturation. The results disclosed a binocular Vernier threshold lower than monocular one (50-60%) providing a better binocular performance similar to contrast detection task. At higher contrasts, the binocular summation in Vernier acuity decreased likely due to saturation. In opposite, Frisen and Lindblom (Frisen and Lindblom, 1988) did not find binocular summation in hyperacuity with a test comparable to Vernier acuity test. In this condition, a large individual variation was shown.

- *Contrast.* Legge described a binocular contrast summation theory in which it is assumed that two monocular channels are summed to provide binocular contrast summation (Legge, 1984b). This valid theory can be take into account in the case of contrast detection, contrast discrimination, dichoptic masking, contrast matching and reaction time studies. It was called quadratic summation and it is defined by the following equation (2):

$$C = \sqrt{(C_L)^2 + (C_R)^2} \tag{2}$$

where C_L and C_R represent the monocular contrast for the left and the right eye, respectively. C is the effective binocular contrast. This equation can be only applied when monocular sensitivities are equal or differ only in contrast (dichoptic stimulation). In some ocular dominance situations, a determined factor must be added to this equation. For instance, in case of contrast detection, a common value of $C=\sqrt{2}$ indicates that monocular threshold is twice the binocular threshold (Legge, 1984a; Anzai et al., 1995). Likewise, in binocular contrast sensitivity function for normal healthy subjects, the same factor of $\sqrt{2}$ is disclosed corresponding to an increase in binocular contrast equal to a 41% (Baker et al., 2007b). On the other hand, as we stated before, binocular contrast summation can vary due to many factors and, equally, it can be inhibited in ocular pathologies as cataract (Pardhan and Elliott, 1991) or amblyopia (Pardhan and Gilchrist, 1992).

2.3. MONOCULAR AND BINOCULAR VISUAL FUNCTION DETERIORATION

2.3.1. Visual acuity and contrast sensitivity

Visual acuity and contrast sensitivity represent two of the most common visual functions taken into consideration in vision assessment. Both can be deteriorated monocularly and binocularly in the case of ocular pathologies as cataract (Pardhan and Elliott, 1991; McElvanney et al., 1994; Pieh et al., 2002), age-related macular degeneration (Midena et al., 1997; Bellmann et al., 2003; Ortiz et al., 2010), optic neuritis (Trobe et al., 1996) or diabetic retinopathy (Stavrou and Wood, 2003), but also after refractive surgeries as keratotomy (Krasnov et al., 1988; Ginsburg et al., 1990; Applegate et al., 1998) or laser-assisted in situ keratomileusis, LASIK (Villa et al., 2009; Anera et al., 2011). In the case of other emmetropization techniques as orthokeratology, Hiraoka et al found that significant decreases in contrast sensitivity monocularly and binocularly under low mesopic illumination. They observed that these deteriorations were correlated with increases in ocular higher-order aberrations depending on the amount of myopic correction (Hiraoka et al., 2008). Age also plays an important role in the degradation of visual acuity and contrast sensitivity (for middle and high spatial frequencies). On the other hand, Bangerter filters and defocus have been widely studied to simulate different degrees of simulated deteriorations in visual acuity and contrast sensitivity. These simulated deteriorations give an opportunity to investigate and understand better clinical implications for the effects on these visual parameters.

Firstly, defocus in vision is defined to the process for which an image is out of focus causing blur on the retina. Defocus is induced through the addition of positive or negative, spherical or cylindrical lenses (accommodation should be taken into account when using negative lenses). So, defocus allows to blur images and generates simulated refractive errors. Defocus curves could be used for evaluating the depth of focus (Pieh et al., 2002). Depth of focus could be useful for verifying the depth of focus especially in bifocal and multifocal intraocular lenses (IOLs) (Weghaupt et al., 1998; Mathur et al., 2015) and also in multifocal contact lenses (Plainis et al., 2013a). An important clinical application of defocus is given for presbyopic correction using monovision technique. Mainly, in monovision, dominant eye is corrected at distance and non-dominant eye at near (with the addition of a positive lens correcting presbyopia). At far, the blurred image of the non-dominant eye will be suppressed and at near, the blurred image of the dominant eye (Jain et al., 1996; Durrie, 2006; Zheleznyak et al., 2015). Several studies highlighted the reduction of the visual acuity proportionally to the amount of positive or negative defocus, especially monocularly (Applegate et al., 1998; Pieh et al., 2002; Weeber et al., 2010; Atchison and Mathur, 2011; Dehnert et al., 2011; Plainis et al., 2011), although positive lenses are preferred to simulate defocus and avoid the accommodation factor on the results. Furthermore, it has been found that defocus affects visual acuity with letters more than for gratings (Thorn and Schwartz, 1990). Other factors affect the degradation of retinal image quality and consequently, visual acuity with defocus as pupil size (Campbell and Green, 1965b; Atchison et al., 1997; Atchison et al., 2005; Weeber et al., 2010), Stiles-Crawford effect (Zhang et al., 1999) and higher-order aberrations (Guo et al., 2008; Atchison et al., 2009;). It is important to specify that deteriorations in visual acuity monocularly and binocularly were worse when defocus and higher-order aberrations (spherical aberrations) had the same signs (Benard et al., 2010; Yi et al., 2011) and less degraded with opposite signs improving depth-of-focus (Applegate et al., 2003; Guo et al., 2008). Nevertheless, binocularly, Plainis et al found that binocular summation in high-contrast visual acuity has been proved to be greater in higher degree of positive defocus-induced blur (+2.00 D) than no defocus in healthy young subjects, although a limitation in this research was the no control of the pupil size. As a reason, they proposed that this improvement could be due to the activation of a larger population of neurons at close-to-threshold detection under binocular stimulation with blurred retinal image (Plainis et al., 2011). In addition, the improvement in visual acuity results from perceptual adaptation to the blurred images (like the restoration of the perceived contrast of the degraded image), which may occur at central sites within the visual cortex (George and Rosenfield, 2004).

Similarly, defocus degrades monocularly and binocularly contrast sensitivity function depending on the degree of defocus and spatial frequencies. Charman found that positive spherical defocus of +1.00 D affected higher spatial frequencies but not spatial frequency of 1 cycle per degree (cpd) (Charman, 1979). Campbell and Green specified that the higher the defocus, the higher the contrast sensitivity deterioration for spatial frequencies above 2 cpd while lower spatial frequencies of 1.5 cpd were degraded for defocus of 2.00 D (Campbell and Green, 1965b). In other work, Pardhan and Gilchrist found in young healthy subjects that with no defocus, binocular contrast sensitivity for a spatial frequency of 6 cpd was approximatively a 42% higher than monocular one but with the increase of monocular blur, binocular performance decreased gradually. For spherical positive defocus of +1.50 D, summation ratio was equal to 1 showing an equal contrast sensitivity for the binocular and monocular viewing while for spherical positive defocus of +2.00, +2.50 and +3.00 D, binocular inhibitions were disclosed (Pardhan and Gilchrist, 1990). Concerning the effects of ocular dominance in middle-aged people, Pekel et al highlighted significant improvement in the dominant eyes respect to non-dominant eyes at a spatial frequency of 18 cpd under mesopic conditions (Pekel et al., 2014). In older adults, under photopic illumination, a loss in contrast sensitivity at high spatial frequencies was reported even without ocular or neurological disease (Derefeldt et al., 1979; Owsley et al., 1983; Owsley and Burton, 1991). At photopic levels, neural changes in the aged visual system contribute little to older adults' loss in spatial contrast sensitivity (Burton et al., 1993).

Secondly, as it is well established, Bangerter foils are widely used to treat amblyopia in children penalizing the non-amblyopic eye and improving the visual acuity of the amblyopic eye (Holmes and Clarke, 2006; Odell et al., 2008; Rutstein et al., 2010). Therefore, Bangerter foils cause progressive deterioration in visual acuity according to the Bangerter values (0.1, 0.2, 0.3, 0.4, 0.6, 0.8, and 1.0). Normally, each value corresponds approximately to the theoretical visual acuity of the penalized eye, in decimal notation (taking into account an initial visual acuity of 1.0 or better). However, Odell et al showed that 1.0, 0.8 and 0.4 foils caused similar minimal degradation in monocular visual acuity at distance and near but also, in Vernier acuity (Odell et al., 2008). Perez et al confirmed similar degradation in monocular visual acuity through 0.8 and 0.4 Bangerter foils (corresponding in their study to mean values of 0.5 and 0.45 respectively). They highlighted the worst degradation in visual acuity with the 0.6 Bangerter foils (mean value in their study equal to 0.35 in decimal notation) (Perez et al., 2010). At last, Li et al found that the 0.8, 0.6, and 0.4 foils had very similar effects to one another in monocular and binocular contrast sensitivity (Li et al., 2012).

Rutstein et al investigated binocular visual acuity in amblyopic and non-amblyopic eyes in 186 children with moderate amblyopia patching with 0.2 and 0.3 foils. They found that these filters degraded non-amblyopic eye sufficiently in amblyopic eyes of the children but the deterioration value was not constant over time (Rutstein et al., 2011). Furthermore, occlusion with Bangerter foils disrupts binocular function more than monocular defocus (Li et al., 2012).

2.3.2. Stereopsis

Stereopsis is of special interest to assess binocular visual performance in vision examinations but also in the clinical practice. Mainly, inducing blur and interocular differences on visual functions, stereopsis is impaired. Monocular or binocular degradations affect stereopsis and, consequently, binocular vision performance.

Monocular image degradation in only one eye produces a worse stereopsis than equally degradations in both eyes. So, progressive increment in monocular degradation involves higher interocular differences causing ocular imbalance between the two eyes and degradation in stereopsis.

For instance, Westheimer and McKee induced blur with positive defocus superior to 2.00 D in normal subjects and controlling the pupil size with artificial pupils of 3 mm in diameter. They observed that blur in one eye and the other without defocus degraded stereopsis more than blur on both eyes (Westheimer and McKee, 1980). In another study, Wood suggested that low spatial frequencies (4 cpd) had a higher effect on the stereoacuity than high spatial frequencies. So, low spatial frequencies impacted worse stereopsis respect to high-spatial frequencies. She corroborated that a mismatch of spatial frequency affected stereothresholds more than when the same spatial-frequency information was received by both eyes (Wood, 1983). Other authors determined the effect of induced monocular blur on different tests measuring stereoacuity in a group of young healthy subjects (Odell et al., 2009). They deteriorated monocular visual acuity by a wide range of Bangerter foils (0.1, 0.2, 0.3, 0.4, 0.8, and 1.0) and they measured stereoacuity using the Randot Preschool Stereoacuity Test, the Distance Randot Stereotest and the Frisby test (the latter producing real depth). They found that stereoacuity thresholds were more negatively affected using the random dot test than with real depth. Li et al confirmed that the effects of four strengths Bangerter foils (0.2, 0.4, 0.6, 0.8) penalized stereopsis in young healthy subjects even more than visual acuity (Li et al., 2012). So et al specified that the size of target influenced stereopsis performance. Analyzing the stereoscopic depth of different Gaussian target (from 1.75 to 28 arcmin), they disclosed that increasing the interocular difference in acuity degraded stereopsis more for small targets than larger ones. In case of large target, stereopsis was modestly affected even if the interocular difference in visual acuity was equal to eight-letter lines (0.8 logMAR) (So et al., 2014).

Other studies investigated how interocular differences in intraocular scattering affected stereopsis. To measure the increase of intraocular scattering, Zhao et al used three scatter filters (Pro Mist ½, Pro Mist 1 and Pro Mist 2) with light transmission of a reduced range equal to 95%, 92%, and 93%, respectively. In these conditions, they found that stereopsis was deteriorated with a binocular increase in scatter levels when applied in both eyes (following the range studied). However, in the presence of interocular differences for a higher scatter level, stereoacuity was degraded even a little more compared to the same scatter levels applied in both eyes (Zhao et al., 2018). On the other hand, Castro et al investigated the impact of interocular differences in higher-order aberrations and Strehl ratio on the maximum disparity (defined as the total range of stereoscopic perception). Under mesopic conditions, their results corroborated deterioration in maximum disparity proportional to the interocular differences in higher-ocular aberrations in normal subjects (Castro et al., 2017). In addition, an important study was performed to understand the consequences on stereopsis after corneal refractive surgery. In their study, Jimenez et al evaluated stereopsis in thirty patients after LASIK surgery. They found that in 83% of the patients, stereopsis was significantly affected after the operation declining on average from 41.1 to 31.3 arc min (Jimenez et al., 2008a).

Thus, it is important to limit interocular differences in visual functions for avoiding disruption in stereopsis and, consequently, binocular vision deterioration.

2.3.3. Phoria and Fusional reserves

General considerations

A complete binocular vergence exam is useful to determine if some binocular abnormalities are present in the subjects. Phorias and fusional reserves are measured to verify the vergence system. Phorias are defined as misalignments or compensated deviations of visual axes due to the fusion reflex (a response to maintain the images received on the foveas of each retina). A fusional reserve is defined as the reserve amount in convergence (visual axes toward nasal) and divergence (visual axes toward temporal) compensating for any phorias relative to a specified distance and, consequently, allowing the fusion reflex (single image perception) to be maintained and avoiding diplopia (double vision). Two baseline studies (Morgan, 1944; Saladin and Sheedy, 1978) determined normal values in phorias and fusional reserves at near and distance in normal subjects (Table 1). These values have been widely discussed throughout the decades. They still are valid values for normal subjects. In older subjects, age affects fusional vergences specially over 61 years' age group at distance for base-in and base-out recovery fusional vergence (Alvarez et al., 2006).

	Phoria and vergences measures (Δ)	
	Morgan's	**Sheedy and Saladin**
Distance		
Horizontal phoria	-1.0 ± 2.0	-1.0 ± 3.5
Horizontal positive vergence		
Blur	9.0 ± 4.0	15.0 ± 7.0
Break	19.0 ± 8.0	28.0 ± 10.0
Recovery	10.0 ± 4.0	20.0 ± 11.0
Horizontal negative vergence		
Break	7.0 ± 3.0	8.0 ± 3.0
Recovery	4.0 ± 2.0	5.0 ± 3.0
Near		
Horizontal phoria	-3.0 ± 5.0	-0.5 ± 6.0
Horizontal positive vergence		
Blur	17.0 ± 5.0	22.0 ± 8.0
Break	21.0 ± 6.0	30.0 ± 12.0
Recovery	11.0 ± 7.0	23.0 ± 11.0
Horizontal negative vergence		
Blur	13.0 ± 4.0	14.0 ± 6.0
Break	21.0 ± 4.0	19.0 ± 7.0
Recovery	13.0 ± 5.0	13.0 ± 6.0

Table 1. Means and standard deviations (±) of the normal values of phoria and vergence measures obtained by Morgan (1944) and Sheedy and Saladin (1978) studies. Δ represents prism diopters.

Another important parameter called vergence facility (VF) could be used to measure the ability of the fusional vergence system to react to a change in vergence (positive and negative). In a normal population, vergence facility may be included between 10 and 15 cycles per minute (cpm) (Gall et al., 1998).

AC/A ratio is defined as the amount of accommodative vergence (AC) induced by a change in accommodation (A). Two ratios can be determined: calculated (3) and gradient (4) AC/A. It is an important factor for the reason that it permits to evaluate the relationship between accommodation and convergence. AC/A ratio is measured in Δ/D (prismatic diopters/diopters), i.e., amount of prismatic diopters put into play by the visual system, for every accommodation diopter.

$$\text{Calculated AC/A } = \frac{15 - \text{distance phoria} + \text{near phoria}}{2.5} \tag{3}$$

$$\text{Gradient AC/A} = |(\text{near phoria with} - 1\text{D}) - \text{near phoria}| \tag{4}$$

In addition, Percival's and Sheard's criteria are calculated to understand if some binocular vision alterations are present, allowing to calculated the prism needed when the corresponding criterion is not met. Percival's criterion is defined as the point-of-zero demand should fall in the middle third of the total fusional vergence. It is a good indicator in the case of eso deviations (Sheedy and Saladin, 1978). If this value is positive, a prism prescription is necessary and the value of the prism is given by the following formula (5):

Prism Needed (Δ) = 1/3 (Greater of blur vergences) – 2/3 (lower of blur vergences) (5)

Sheard's criterion is defined as the amount of the heterophoria should be inferior to half the opposing fusional vergence in reserve. In opposite of Percival's criterion, it is more indicated for exo deviations (Sheedy and Saladin, 1978). If the value is higher than 0, a prism needs could be prescribed following the formula (6):

Prism needed (Δ) = 2/3 (phoria) - 1/3 (compensating fusional vergence) (6)

So, when a phoria is decompensated, retinal images do not fall into the Panum's fusional area causing visual discomfort, asthenopia, strabismus, amblyopia and mainly, deterioration in binocular vision performance. For instance, children with intermittent exotropia have convergence fusional reserves at distance limited and lower than normal mean values (Hatt et al., 2011).

Binocular dysfunctions	**Fundamental signs**	**Complementary signs**
Convergence insufficiency	High exophoria at near (≥6Δ) greater than at far	Low AC/A ratio (<3/1) Reduced PFV at near(≤ 11/14/3 Δ) VF ≤ 13 cpm (difficulty with 12Δ Base out prism)
Convergence excess	Significative esophoria at near (≥ 1 Δ), greater than at far	High AC/A ratio (>7/1) Reduced NFV at near (≤ 8/16/7 Δ) VF ≤ 13 cpm (difficulty with 3Δ Base in prism)
Divergence excess	Significative exophoria at far (≥ 4Δ), greater than at near (the difference must be > 5Δ)	High AC/A ratio (>7/1) Reduced PFV at far(≤ 4/10/5 Δ) Reduced PFV at near(≤ 11/14/3 Δ) VF ≤ 13 cpm (difficulty with 12Δ Base out prism)
Basic esophoria	Significative esophoria at far and near of equal amount (deviations within 5Δ of one another are considered equal)	Reduced NFV at far (≤ X/3/1Δ) Reduced NFV at near (≤ 8/16/7 Δ) VF ≤ 13 cpm (difficulty with 3Δ Base in prism)
Basic exophoria	Significative exophoria at far and near vision of equal amount (deviations within 5 Δ of one another are considered equal)	Reduced PFV at far (≤ 4/10/5 Δ) Reduced PFV at near (≤ 11/14/3 Δ) VF ≤ 13 cpm (difficulty with 12Δ Base out prism)
Fusional vergence dysfunction	PFV and NFV reduced at far and near	VF ≤ 13 cpm (difficulty with 3 Δ base in and 12 Δ base out)

Table 2. Clinical signs in binocular dysfunctions. NFV= Negative Fusional Vergence. PFV= Positive Fusional Vergence. VF= Vergence Facility.

On the other hand, several binocular visual problems due to binocular dysfunctions can occur as convergence insufficiency, convergence and divergence excess, basic esophoria and exophoria and fusional vergence dysfunction (Table 2). In Table 2, the main binocular dysfunctions are described for young healthy people (university students). Convergence insufficiency represents one of the most common vergence abnormalities in the population affecting negatively near vision (Rouse et al., 1999; Scheiman et al., 2005). Divergence insufficiency is not represented for the reason that could only occur in older adults.

Some factors could influence vergence performance. In myopic young people, the use of spectacles respect to contact lenses cause poorer accommodative and vergence function (Jimenez et al., 2011). Then, horizontal disparity causes vergence errors inducing forced vergence demands and consequently, degradation in vergence function and stereopsis (Ukwade et al., 2003) while vertical disparity decreased negative horizontal fusional reserves (blur, break and recovery) and positive fusional reserves in break (Momeni-Moghaddam et al., 2017).

2.3.4. Light scattering and retinal image quality

Mainly, light entering in the eye, which spreads through different ocular media (cornea, aqueous humour, crystalline lens and the vitreous humour), is scattered due to the interaction with proteins, collagen fibers, ocular membranes, etc. This scattered light is called forward scattering. The phenomenon of induced intraocular scattering causes a veiling luminance on the retina influencing retinal image quality: the higher the veiling luminance the lower the retinal image quality (Castro et al., 2010). The increment of intraocular scattering produces ocular straylight (van den Berg et al., 2013) and, in consequence, visual disturbances such as disability glare or night vision symptoms (halos). Glare is formed by disability glare and discomforting glare where disability glare cause a reduction of visual performance (contrast sensitivity), while discomforting glare does not impact the performance of visual function (Abrahamsson and Sjostrand, 1986; van Rijn et al., 2005). A halo is defined as a dim disc of light surrounding the image of a point luminous source inducing visual discomfort (Obrart et al., 1994; Allen et al., 2008; Castro et al., 2011). Straylight is defined as the visual effect of intraocular scattering. Indeed, straylight phenomenon is produced due to light radiations are observed while a bright light is projected on a dark background (van den Berg et al., 2013). According to Commission Internationale d'Éclairage (CIE), straylight corresponds to the peripheral part of a point spread function (PSF) and can be calculated by the following equation (7) (van den Berg et al., 2013):

$$s = \theta^2 \, x \frac{L_{eq}}{E_{bl}} = \theta^2 \, x \, PSF \tag{7}$$

where s represents straylight, θ light scattered angle, L_{eq} equivalent luminance, E_{bl} intraocular illuminance (lm/m^2). Normally, to quantify experimentally the straylight, it is common to evaluate logarithm straylight log(s) measured by a device called C-Quant which uses a compensation comparison method (Coppens et al., 2006).

On the other hand, to assess halos size, different devices can be used such as the Halo test (Castro et al., 2014a). or the Light Disturbance Analyzer (Villa et al., 2007). These two devices are well described in the Chapters 3 and 5, respectively. But basically, these tests consist of detecting luminous peripheral stimuli around a central high-luminance stimulus over a dark background

As we stated, retinal image quality depends strongly on intraocular aberrations and scattering. The latter two being in turn are influenced by several important factors like diffraction, pupil diameter, age and ocular media transparency. Age and ocular media transparency are strongly correlated. With age, ocular media transparency is altered, impairing retinal image quality (Artal et al., 1993), higher aberrations, higher scattering like in cataract eyes (Van den Berg et al., 2007) and, therefore inducing contrast sensitivity degradation (Van Den Berg et al., 1989; De Waard et al., 1992; de Wit et al., 2006; Lorente-Velazquez et al., 2011b; Patterson et al., 2015). In cataract eyes, light scattering is one of the main cause of image degradation due in part to lens opacity (Sahin et al., 2016).

Diffraction is limited by pupil diameter, which determines the quantity of light entering in the eye: the higher the pupil size, the higher the intraocular scattering and the higher the aberrations leading to a deterioration of the retinal image quality. For instance, in normal eyes, when the pupil is inferior to 3 mm, irregular aberrations (like defocus, astigmatism, coma, and spherical aberration) do not have a large effect on retinal image quality but, if the pupil diameter is superior to 7.3 mm, negative effects are reported on the optical quality (Liang and Williams, 1997). In addition, with the increase of pupil diameter, night vision disturbances as halos raise due to higher scattering produced by glare worsening optical quality (Castro et al., 2014a). As a consequence of the intraocular scattering increase, modulation transfer function (MTF) and, therefore, contrast sensitivity, impair (Perez et al., 2009).

Optical quality can be quantified objectively through different parameters. Several works have used metrics such as higher-order aberrations using an aberrometer, and the Objective Scattering Index (OSI), the Strehl ratio, and the Modulation Transfer Function cutoff (MTF cutoff) using a double pass device called OQAS II (Optical Quality Analysis System II, Visometrics, Tarrasa, Spain). The latter has been widely used in clinical practice to assess retinal-image quality (Jimenez et al., 2008c; Anera et al., 2011; Ondategui et al., 2012; Xiao et al., 2015; Hwang et al., 2018b). This device will be described in Chapter 3. Several parameters can be measured such as mean OSI to assess tear film quality, OSI, MTF cutoff, Strehl ratio, etc. Mainly, the OSI quantifies the intraocular scattering: the higher the OSI, the lower the retinal-optical quality. The MTF cutoff represents the spatial frequency corresponding to a theoretical MTF value of 0 (the noise produced by the CCD camera is considered in the calculation of the parameter), and the Strehl ratio, which corresponds to the 2D-MTF area of the eye and the diffraction-limited 2D-MTF area (the higher the Strehl ratio, the lower the intraocular scattering and ocular aberrations).

Several studies investigated the effect of scattered light on different ocular pathologies or after ocular surgery showing how the retinal image quality is impaired by increases of intraocular scattering and straylight, as occurs in cataract (De Waard et al., 1992; Valbon et al., 2013; Xiao et al., 2015; Paz Filgueira et al., 2016; Martinez-Roda et al., 2019) or ARMD and keratitis (Castro et al., 2011). Refractive surgery also can negatively affect retinal image quality by the increment of straylight and light scattered, as occurs in photorefractive keratectomy (PRK) or LASIK (Ondategui et al., 2012) or even after cataract surgery (Martinez-Roda et al., 2011; Xiao et al., 2015; Paz Filgueira et al., 2016), although it is clear that these surgery processes resolve other visual or ocular disorders.

As stated previously, to simulate different degrees of intraocular scattering and retinal image degradation, several filters can be used, in addition to defocus. Bangerter foils have been widely used to occlude the non-amblyopic eye in amblyopia therapy (Rutstein et al., 2011). It has been also proved that fog filters as BlackProMist 2 can simulate an early cataract (de Wit et al., 2006). Taking into account these considerations, it has been well established that: the higher the intraocular scattering induced by filter, the higher the straylight and glare, and the lower the retinal optical quality (de Wit et al., 2006; Perez et al., 2010; Barrionuevo et al., 2010; Martinez-Roda et al., 2019). Also, night vision disturbances as halos, straylight and glare are affected negatively degrading retinal image quality (Castro et al., 2011; Cinta Puell and Palomo-Alvarez, 2017).

2.4. INFLUENCE OF ALCOHOL CONSUMPTION ON BINOCULAR VISUAL PERFORMANCE AND DRIVING DEGRADATION

2.4.1. Visual impairment

Alcohol (or ethanol) is a psychoactive substance acting and depressing central nervous system, reducing the speed of neuronal processing and, in addition, decreasing neuronal transmission (Khan and Timney, 2007). In these circumstances and depending on the quantity of alcohol ingested, apart from other factors, overall visual function is prejudiced by this substance. As it is well established, alcohol content varies with weight, biological sex, age and alcohol practice (Casares-Lopez et al., 2021). In continuation, we will discuss on the consequence of alcohol consumption in several visual parameters such as visual acuity, contrast sensitivity, phorias and fusional vergences, stereopsis, retinal-optical quality and night-vision disturbances.

Firstly, visual acuity could be affected for high alcohol content but it seems to not show significant deteriorations for moderate to low doses in healthy subjects. Several studies proved that at distance, visual acuity is affected negatively by alcohol intake, although only for high blood alcohol content or blood alcohol concentration (BAC), taking a mean value of 0.06%. However, no significant deteriorations were found in near visual acuity (Wilson and Mitchell, 1983) . Another study confirmed the tendency that binocular visual acuity at distance was deteriorated only for high alcohol content corresponding to a Breath Alcohol content (BrAC) equal to 0.10%, while a BrAC equal to 0.05% did not show significant differences (Watten and Lie, 1996). Pearson and Timney disclosed small significant deteriorations monocularly and binocularly at near but, at far, higher deteriorations were found more monocularly than binocularly with alcohol consumption (BAC=0.06%) (Pearson and Timney, 1998). The negative influence of alcohol in visual acuity was studied also in people suffering diabetic retinopathy with moderate and high alcohol content confirming deterioration in this visual parameter with alcohol consumption (Lee et al., 2010).

Secondly, the effect of different alcohol levels in contrast sensitivity has been studied in low and high spatial frequencies in young healthy subjects. Under photopic conditions, Adams et al found significant deterioration in low spatial frequencies with moderate and high alcohol levels (BAC=0.05% and 0.10%)

(Adams et al., 1976). Considering BrAC levels of 0.05% and 0.10%, Watten and Lie found also significant impairment with both contents in contrast sensitivity (mean contrast of the optotypes was 0.96) for high spatial frequencies (12 and 18 cpd) but not for 1.5, 3, and 6 cpd (Watten and Lie, 1996). Regarding static and dynamic contrast sensitivity, several studies investigated the effect of alcohol consumption on different spatial frequencies (static and moving targets). Andre et al found significant degradations with the effect of a high alcohol content (mean BAC = 0.09%) in both contrast sensitivity (static and dynamic) and for all spatial frequencies measured (1.5, 3, 6, and 12 cpd) being worse in dynamic contrast sensitivity (Andre et al., 1994). They repeated this experiment with a high BAC of 0.07% and varying the luminance and glare. They corroborated significant deteriorations with alcohol consumption for all spatial frequencies investigated (1.5, 3, and 6 cpd) (Andre, 1996). In addition, in lower alcohol consumption, Nicholson et al also studied static and dynamic contrast sensitivity but with two lower intakes (mean BAC = 0.01 and BAC = 0.04) at spatial frequencies: 1, 6, and 12 cpd (static and dynamics targets). Similarly, they disclosed significant impairment at all spatial frequencies for the moderate BAC equal to 0.04% but not in case of low BAC (0.01%) (Nicholson et al., 1995). Pearson and Timney disclosed significant impairments at all spatial frequencies (0.5, 0.75, 1, 2, 4, 6, 8, 12, and 14 cpd) being higher in low and high spatial frequencies respect to central spatial frequencies for an alcohol content (BAC) of 0.06% (Pearson and Timney, 1998). Recently, in a larger group of participants (40 subjects), Casares et al studied the effect of contrast sensitivity for two BrACs (low-BrAC = 0.18 mg/l and high-BrAC = 0.28 mg/l). They found out monocularly significant differences at spatial frequencies of 6, 12, and 18 cpd in the low-BrAC group and 0.75, 1.5, 3, 6, and 12 cpd for the high-BrAC, while binocularly, significant deteriorations were highlighted for 6 and 12 cpd spatial frequencies (for high BrAC) and 12 cpd for low BrAC (Casares-Lopez et al., 2020a).

Thirdly, phorias, fusional vergences and stereopsis are affected by alcohol consumption. Several studies revealed changes in lateral phorias with alcohol intake postulating that in young healthy people with normal binocular vision, phorias become more esophoric at far and more exophoric at near. One of the first studies on binocular vision and alcohol was conducted by Colson which had observed in horizontal phoria at far changing towards esophoria with alcohol consumption (Colson, 1940). Brecher et al investigated in-depth binocular vision in young healthy subject through vergence system. He observed diplopia for a BAC of 0.10% due to reduction of fusional reserves, increase in esophoria at far (6 m) and exophoria at near (33 cm), but no difference in vertical phoria. He explained these changes and diplopia by progressive deterioration of the binocular fusion reflex and the weakening of voluntary convergence. This could be cause by an impairment of the general neuromuscular coordination (Brecher et al., 1955).

McNamee confirmed that horizontal phorias at far became more esophoric and no change in vertical phorias at far with high BAC of 0.08% (McNamee et al., 1981) suggesting an ease on the sensitivity of horizontal ocular muscles respect to vertical plane (Fender, 1964). Miller et al observed decreases in positive and negative fusional vergence with alcohol consumption (BAC = 0.08%) (Miller et al., 1986) and confirmed intoxication with alcohol consumption of BAC equal to 0.06% in lateral phoria increasing esophoria at far (Miller, 1991). In the same way, Hogan and Linfield showed significant increase in esophoria at 6 m with a reduction in the negative fusional ability, and an increment in exophoria at near with a decrease in the AC/A ratio with moderate doses of ethanol (Hogan and Linfield, 1983). Regarding AC/A, several years before, Cohen and Alpern had observed a significant decrease in response AC/A proportional to the level of blood ethanol (Cohen and Alpern, 1969). Most recently, Munsamy et al investigated the influence of two alcohol intakes: BAC of 0.05% and 0.10% corroborating previous studies: for lateral phorias, an increase in esophoria at far and an increase in exophoria at near, a reduction in the positive and negative fusional vergences at far and near, and an impairment in near point of convergence proportional to the quantity of consumed alcohol. So, changes were always significant and higher for a BAC of 0.10% compared to a BAC of 0.05% (Munsamy et al., 2016).

Regarding the effect of alcohol on stereopsis, it is reasonable to suppose that stereopsis at far is removed by diplopia caused by alcohol consumption in any event. It seems that a lack of study exists quantifying the degradation of stereopsis with the amount (low or high) of alcohol consumption. However, some studies investigated stereopsis at near. For instance, Wilson and Mitchell did not found significant deteriorations with a mean BAC equal to 0.06% in the stereopsis at near (33 cm) measured with Titmus Test (Wilson and Mitchell, 1983). Contrariwise, Watten and Lie found significant deteriorations in two levels of alcohol (BAC of 0.05% and 0.10%) measuring stereoacuity at near using the same test (Polaroid Vectogram, Titmus test). To the best of my knowledge, no study has investigated the effect of alcohol on vergence facility being an interesting point to take into consideration.

Finally, retinal image quality and night vision disturbances could be deteriorated by alcohol consumption increasing the amount of intraocular scattering (Casares-Lopez et al., 2021). In this regard, Castro et al investigated the effect of alcohol consumption in retinal-image quality and night-vision disturbances in a healthy cohort of 56 participants between 20 and 59 years with a mean age of 26 years. Under alcohol consumption, they quantified tear film stability, MTF cut-off with a double-pass device used to assess retinal image quality, pupil size, and visual disturbance index (VDI). The latter measured the halo size under low-illumination conditions. They found significant increases in VDI (monocularly and binocularly) and pupil size, and a decrease in the MTF cut-off, but also a deterioration in the tear film stability under alcohol consumption (mean BrAC = 0.32 mg/l), highlighting the deterioration of the visual discrimination capacity (higher halo size with alcohol intake) and, consequently, an impairment of night vision. They supposed that this could be due to the higher pupil size and the tear film deterioration reached with alcohol consumption, which provoked an increment of the ocular aberrations and intraocular scattering entering in the eye causing a degradation of the retinal-image quality and, therefore, the increment of visual disturbances. Separating into two groups, BrAC ≤ 0.25 mg/l and BrAC ≥ 0.25mg/l, they found proportional impairment with alcohol in these visual parameters measured: the higher the BrAC, the higher the binocular VDI deterioration and the consequent higher night vision alterations (Castro et al., 2014a). In other of their studies, Castro et al confirmed deterioration in night vision performance through increase in VDI with alcohol consumption (mean BrAC = 0.30 mg/l). In their study, they evaluated the optical quality using the OQAS II device through two visual parameters (Strehl Ratio and OSI) in 67 healthy young subjects (mean age 27.6 years) separating them in two groups after alcohol intake: BrAC ≤ 0.25 mg/L (mean BrAC of 0.19 mg/l) and BrAC ≥ 0.25 mg/l (mean BrAC of 0.38 mg/l). They showed a significant decrease in Strehl ratio proportional to the amount of alcohol consumed and a significant increase in OSI (but only in the group with BrAC ≥ 0.25mg/l) disclosing that the higher the BrAC, the higher the deterioration in retinal image quality and the higher the perception of dysphotopsias (such as halos) (Castro et al., 2014b). Recently, Casares et al studied the effect of alcohol consumption on retinal straylight in 40 healthy subjects (mean age 28.4 years) separating them in two groups: BrAC ≤ 0.25 mg/l and BrAC ≥ 0.25 mg/L. They assessed retinal straylight through the log(s) parameter. They found a significant increase in log(s) for both groups being the greater deterioration for the group with a BrAC ≥ 0.25 mg/l. They highlighted that intraocular scattering and related straylight (assessing the forward scattered light in the retina) increased with alcohol consumption (Casares-Lopez et al., 2020a).

2.4.2. Driving deterioration

Driving is a complex task involving several factors such as controlled behavior (control over speed, braking and lane position), concentration, attention, capacity to react quickly to decision-making, high processing through the central nervous system and, obviously, sufficient visual performance. It is also known that alcohol can induce sleepiness during driving.

As it is well established, alcohol consumption affects negatively these factors compromising considerably driver safety and driving surrounding conditions (pedestrian, transportation…). The influence of alcohol consumption on driving has been well documented in the literature. Alcohol is the most frequently detected substance in fatal traffic accident. Most studies used a driving simulator to investigate effectively the impact of alcohol intake on driving, although there is not a consensus on the validity of this device. Some studies concluded that simulator cannot be adequate because it is not like real driving and participants could drive with less attention than in real condition or due to sickness induced by simulator (Kawano et al., 2012; Helland et al., 2016). Opposite, others studies established that recent driving simulators represented an accurate dispositive to analyze driving-related parameters (Iwata et al., 2021; Shechtman et al., 2009) such as reaction time, standard deviation of the lateral position, speed, collisions, steering wheel control, or attention.

Firstly, reaction time has been widely studied with different alcohol content showing higher reaction time. One of the first studies using a car simulator to investigate reaction time was implemented by Allen et al on 18 licensed drivers (age range;21-65 years) at blood alcohol content (BAC) of 0.06 and 0.10%. For both levels of alcohol consumption, reaction times were found to be higher proportionally to alcohol consumed (Allen et al., 1975). In other study, Wester et al investigated different BAC levels (0.02, 0.05, 0.08 and 0.10%) in 32 healthy participants (16 men and 16 women) between 21 and 50 years old. They found significant increase in reaction time respect to placebo condition in the two high BAC (0.08 and 0.10%) for a dual-task driving. In addition, significant higher reaction times were found in moderate and high BACs (0.05, 0.08 0.10%) for a single task driving (Wester et al., 2010). Christoforou studied the effect of a large range of BrAC in young drivers. They highlighted an increment in reaction time under alcohol consumption and they specified that reaction time were one of the most reliable alcohol indicators (Christoforou et al., 2012). In addition, Banks et al studied the effect of a low BAC of 0.035% and sleep deprived (5 hours of night sleep) in 20 healthy volunteers (mean age of 23 years). They disclosed significant increase in the reaction time in these subjects under the effect of this alcohol intake.

Secondly, several studies revealed higher speed under different doses of alcohol consumption. Allen et al studied the effect of a moderate alcohol dose (BAC) equal to 0.055% in 33 subjects highlighting an increment in speed of 30% under alcohol consumption (Allen et al., 1996). Mets et al investigated the standard deviation of speed (SDSP) which represents a value of the variability in speed through a determined simulated car circuit. A total of 27 young subjects participated in this investigation under three different alcohol contents, from moderate to high alcohol consumption (BAC of 0.05%, 0.08%, and 0.11%). Respect to placebo condition, significant increases were obtained for BACs of 0.08 and 0.11%, but not for the BAC of 0.05% (Mets et al., 2011). Irwin et al conducted a systematic review and meta-analysis of the available evidence on standard deviation of speed (SDSP) finding a significant increment in this parameter under the effect of alcohol (SDSP = 0.38 km/h). As stated before, Christoforou indicated, along with reaction time, that speed is an accurate indicator to measure deterioration in simulated driving finding a significant speed increase with alcohol consumption, although the BrAC speed curve was not monotonic over all the range of BrACs measured (Christoforou et al., 2012). A study conducted by Vollrath and Fischer under the influence of alcohol (BAC = 0.05%) specified an interesting point. They showed that drivers seemed to lower their speed when the simulated scenarios were complex and difficult possibly due to counteract alcohol effects. Nevertheless, in easy scenarios, they were more confident in their driving and the arousing effect of alcohol may contribute to driving faster (Vollrath and Fischer, 2017).

Thirdly, Standard Deviation of the Lateral Position (SDLP) is an important factor to take into consideration in driving performance. It corresponds to the variability of the vehicle lateral position in simulated driving: the higher the SDLP, the poorer the lateral position control in simulated driving. Several studies proved significant increment under different alcohol consumption doses. Berthelon and Gineyt measured the SDLP parameter with a driving simulator through different scenarios such as road tracking, car following, and an urban scenario including events inspired by real accidents in sixteen experienced drivers and under three low-high BAC: 0.03, 0.05 and 0.08%. They found an increment and deterioration in SDLP under alcohol consumption being notable with the highest dose (Berthelon and Gineyt, 2014). Other authors confirmed the same results for the SDLP measuring with the same doses of alcohol (Charlton and Starkey, 2015). Helland et al confirmed, in a cohort of 20 healthy men volunteers, a significant increase in SDLP under a high BAC of 0.09% but not significant under a BAC of 0.05% suggesting, according to their results that, SDLP in the driving simulator is a sensitive measure of alcohol consumption in impaired driving, despite the SDLP is amplified in the simulator respect to real driving (Helland et al., 2013). Mets et al found significant increase in SDLP in twenty-seven healthy young subjects under three moderate-high alcohol consumption with BACs of 0.05,0.08, and 0.11% (Mets et al., 2011). Freydier et al investigated the effect of alcohol with a BAC of 0.05% and the driving experience. To this end, they separated in novice (driving license inferior at two months and less than 5,000 km driving) and experienced drivers (corresponding to drivers with driving license superior to three years and more than 20,000 kilometers driving) two groups of sixteen students. They found that SDLP was increased with alcohol consumption being higher in novice drivers compared to experienced drivers. They confirmed that SDLP was a valid indicator referred to impaired behavior with alcohol consumption (Freydier et al., 2014).

Fourthly, number of collisions is an important and paramount factor to take into account when we assess driving under the influence of alcohol due to its concrete, fatal injuries and serious implications in crash driving (Zador et al., 2000). The relative risk of being involved in a fatal crash as a driver is four to 10 times greater for drivers with BACs between 0.05 and 0.07% compared to drivers without alcohol intake (Fell and Voas, 2009). As it is well established, this parameter is degraded depending on the quantity of alcohol consumption. Vakulin et al studied the effect of low BAC (0.025 and 0.035%) with and without sleep deprivation (four hours in sleep) in twenty-one healthy young men. They found that the number of collisions was the highest in the group with BAC of 0.035% and sleep deprivation (Vakulin et al., 2007). Vakulin et al confirmed the results of Banks et al that had found collisions increases and reduction in driving performance under the effect of alcohol equal to a low BAC of 0.035% and sleep deprived (5 hours of night sleep) in 20 healthy volunteers with a mean age of 23 years (Banks et al., 2004). Bloomberg et al highlighted that a significant increase in relative risk of collisions were observed at BACs between 0.04 and 0.05% and becoming very elevated when BACs were superior to 0.10% (Blomberg et al., 2009).

Finally, steering control represents an important parameter to investigate for understanding the influence of alcohol on driving control. Several studies highlighted impairment in steering control. Van Dyke and Fillmore studied this parameter in 50 healthy experienced drivers (36 men and 14 women) taking in consideration a BAC equal to 0.065%, which is below the legal limit in the USA (0.08%). They disclosed that even with this BAC steering rate and driving performance were deteriorated significantly (Van Dyke and Fillmore, 2015). Even for a BAC of 0.055%, Allen et al found a significant increase in steering rate inducing less control in driving in thirty-three healthy experienced drivers (Allen et al., 1996). As cited above, in its investigation on moderate sleep deprivation and low-dose of alcohol, Vakulin et al showed that steering deviation increased significantly when participants had sleep deprivation and low dose of alcohol (Vakulin et al., 2007).

CHAPTER 3

Visual performance after the deterioration of retinal image quality: induced forward scattering using Bangerter foils and fog filters (Study 1)

This study has been published in the journal *Biomedical Optics Express* (Castro-Torres et al., 2021).

3.1. INTRODUCTION

In recent years, research into retinal-image quality has increased, mainly due to its clinical applications, especially in terms of refractive and cataract surgery (Alio et al., 2008; Ondategui et al., 2012; Xiao et al., 2015; Liu et al., 2019) and ocular pathologies (Van den Berg et al., 2007; Ortiz et al., 2010; Artal et al., 2011; Castro et al., 2011; Vilaseca et al., 2012a). The characterization of the eye in older adults is another important clinical application, considering the age-related deterioration of the ocular media (Van den Berg et al., 2007; Martinez-Roda et al., 2016a). It is well known that the optical conditions of the ocular media have an important effect on the retinal-image quality of the human eye. In fact, light scattering through the ocular media is the most important cause of retinal-image degradation, especially in eye diseases such as cataracts (Vilaseca et al., 2012a; Ortiz et al., 2013a). In the presence of a light source, light is scattered when passing through the ocular media, leading to increased straylight. This amplification of scattered light may produce certain visual disturbances caused by the straylight, especially under low-illumination conditions, such as disability glare (Patterson et al., 2015), thus reducing night-vision performance. In disability glare, the visual field luminance is greater than that for which the eyes are adapted, causing annoyance and discomfort (Fan-Paul et al., 2002). Moreover, intraocular straylight induced by light scattering reduces the overall contrast of the retinal image and, consequently, some visual functions, such as contrast sensitivity (Lorente-Velazquez et al., 2011b; Cinta Puell and Palomo-Alvarez, 2017) and visual discrimination capacity (halo perception) (Ortiz et al., 2013a; Casares-Lopez et al., 2020a) are deteriorated. These negative effects are more evident when the source of glare is present within the visual field (Franssen et al., 2007). Some studies have found a greater deterioration in eyes with a poorer retinal-image quality (Ortiz et al., 2010; Castro et al., 2011; Martinez-Roda et al., 2016a; Paz Filgueira et al., 2016). Most previous work is focused on the study of visual acuity and contrast sensitivity. There has been scant analysis of other important visual functions, such as glare sensitivity, halo perception, and visual discrimination capacity. However, as we have mentioned, intraocular scattering and straylight produce important visual disturbances, especially under conditions of glare or in dim surroundings, which could have repercussions on daily tasks like driving (Casares-Lopez et al., 2020a). For this reason, quantifying positive dysphotopsias such as glare, halos, and starbursts, is particularly interesting for both research and clinical purposes (Anera et al., 2011; Puell et al., 2014; Patterson et al., 2015; Cinta Puell and Palomo-Alvarez, 2017).

On the other hand, from a clinical perspective, it is interesting to analyze, in the same patient, how different levels of retinal-image degradation influence visual performance, as well as the correlation between retinal-image quality and visual function. In this sense, simulating the degradation of retinal quality is a useful tool for research purposes with potential clinical applications, particularly for evaluating visual function and ocular parameters, and studying and monitoring several ocular pathologies de Wit et al., 2006; Odell et al., 2008; Ikaunieks et al., 2009; Anderson et al., 2009). In order to quantify and evaluate visual performance, including the characterization of dysphotopsias (glare, halos, etc.), filters like Bangerter foils, and certain camera fog filters, can be used to simulate different levels of retinal image quality degradation. Bangerter foils are widely used as occlusions for penalization in children undergoing amblyopia therapy (Stewart et al., 2004; Rutstein et al., 2010;). Some authors have used Bangerter foils to optically characterize the eye or simulate optical degradation (Odell et al., 2008; Odell et al., 2009; Perez et al., 2010). In addition, some camera fog filters have been proved to simulate incipient and moderate cataracts, due to the induced forward scattering (de Wit et al., 2006; Hwang et al., 2018a; Martinez-Roda et al., 2019).

In this study, we induced and evaluated different levels of retinal-image degradation by increasing forward scattering, using several Bangerter foils and fog filters. In addition, we studied the influence of this retinal-image degradation on visual performance by means of visual acuity, contrast threshold (under normal and glare conditions), straylight, and visual discrimination capacity (perception of halos). To this end, we also analyzed possible correlations between night-vision performance and retinal-image quality.

3.2. METHODS

3.2.1. Subjects

A total of 7 subjects (fourteen eyes) were enrolled in the experiment (3 females, 4 males) with a mean age of 27.7 ± 6.5 years. The admission criteria for the subjects were: decimal visual acuity ≥ 1.0 with the best correction for both eyes, and no pathological conditions or pharmacological treatments that could affect visual performance. All participants gave their informed consent in accordance with the Helsinki Declaration, and the study was approved by the Human Research Ethics Committee of the University of Granada (921/CEIH/2019). Corrected distance visual acuity (CDVA) was measured at a working distance of 5.5 m using the Pola VistaVision Visual Acuity Chart System (DMD Med Tech, Torino, Italy). The participants performed the visual tests using their best optical correction.

3.2.2. Filters

In order to analyze different levels of deterioration in the retinal-image quality, we used several filters. Five Bangerter foils (Ryser Optik, St Gallen, Switzerland) were used to worsen the retinal-image quality, graded 0.8, 0.6, 0.4, 0.3, and 0.2. Each value corresponds approximately to the theoretical visual acuity of the eye, in decimal notation, when seeing through the foil (taking into account an initial visual acuity of 1.0 or better). These foils present a pattern of microbubbles which produces the image degradation. Bangerter foils 0.8, 0.6, 0.4, 0.3 and 0.2 are characterized by a bubble density of 3.40, 3.41, 3.76, 3.44, and 4.32 bubbles/mm^2, respectively. They also present a bubble diameter of 0.26, 0.41, 0.22, 0.33, and 0.44 mm, respectively. Bangerter foils are of interest as they are employed in ocular penalization in children undergoing amblyopia therapy (Rutstein et al., 2010; Stewart et al., 2004). In addition, these filters are used to simulate visual degradation (Odell et al., 2008; Odell et al., 2009; Perez et al., 2010; Kingsnorth et al., 2016; Molina et al., 2021). We also included different fog filters used in photography: the Black ProMist2 (Tiffen, Hauppauge, NY), the Fog A and the Fog B filters (HOYA, Kenko Tokina Co., Tokyo, Japan), a combination of the Fog A and Fog B filters (Fog_A+B), and the Fog_1 filter (B+W, Schneider, Bad Kreuznach, Germany). The structure of these filters is mainly characterized by their grain: the Fog_1 filter presents the smallest grain size, as well as the smallest grain density, and the Black ProMist 2 has the largest grain size but also greater variability in terms of the size and form of the grain. The Fog B filter produces a stronger fog effect than Fog A, which has a larger grain size. These camera filters, which produce an effect similar to dense fog, have been proved to provide visual acuity and contrast sensitivity values that can be used as cataract-simulating filters (de Wit et al., 2006). The Bangerter foils were fixed on ophthalmic lenses, with no optical power, previously mounted on eyewear frames: for each filter, a frame with the Bangerter foil affecting one eye was used. The fog filters were assembled on Knobloch K-2 shooting glasses (Knobloch Optik GmbH. Karlsruhe, Germany). To do this, a filter adapter was fitted onto the corresponding lens-holder of the shooting glasses. This frame allowed us to properly place the lens-holder with the fog filter in front of the eye. All the filters were analyzed beforehand, using an artificial eye used to calibrate the WASCA aberrometer (Carl Zeiss Meditec, AG, Germany), with a refractive error of +3.74D.

3.2.3. Retinal-image quality

Retinal-image quality was characterized using the OQAS II (Optical Quality Analysis System II, Visiometrics, Terrassa, Spain), a double-pass device widely validated in clinical practice (Ortiz et al., 2010; Vilaseca et al., 2012a) which uses an infrared laser diode (780 nm) as light source to obtain the double-pass images. The parameters measured were the Objective Scatter Index (OSI) and the Strehl ratio. The OSI parameter is obtained by analyzing the retinal image of a point source of light, calculated as the ratio between the light intensity within an annular area of 12 and 20 arc min and the intensity of the central peak (within 1 arc min) of the double-pass image (Artal et al., 2011). This parameter is measured for a pupil diameter of 4 mm. The OSI objectively quantifies the intraocular scattering affecting the retinal image in such a way that a high OSI value indicates a greater contribution of intraocular scattering. OSI values lower than 1.0 correspond to normal eyes whereas cataractous eyes present OSI values of 1.0 and higher. The Strehl ratio provides information on the overall optical-quality and is defined as the ratio between the 2D Modulation Transfer Function (2D-MTF) area of the eye and the diffraction-limited 2D-MTF area. This parameter ranges from 0 to 1, where the higher the value, the fewer the ocular aberrations and scattering and, therefore, the better the retinal-image quality.

Figure 6. Artificial eye fixed to the OQAS device to measure optical quality.

We first measured the optical quality of the artificial eye under normal conditions (without a filter). To do this, the artificial eye was fixed to the OQAS chinrest (Figure 6), following the manufacturer’s instructions for the calibration process. We also measured the optical quality of the system comprising the artificial eye and a filter, for all the Bangerter foils and fog filters. We took three measurements and averaged these for each experimental condition. The data corresponded to a pupil diameter of 5 mm (Strehl ratio) and 4 mm (OSI). After this, both eyes of each participant were examined under natural conditions (with no filter), in addition to the system comprising the subject eye and a filter, for all the eyes and all the filters described (Bangerter foils and fog filters).

3.2.4. Visual discrimination capacity (halo perception)

The visual discrimination capacity under low ambient lighting was evaluated using the Halo test (http://hdl.handle.net/10481/5478, University of Granada, Granada, Spain), which is a visual test based on the freeware software Halo v1.0 (Castro et al., 2014a) presented on a LCD-monitor. This test has been successfully used in clinical applications for ocular pathologies (Castro et al., 2011; Ortiz et al., 2013b), after refractive surgery (Anera et al., 2011), and under different experimental conditions (Castro et al., 2014b; Castro et al., 2016). The test consists of detecting peripheral luminous stimuli (35 cd/m^2) around a central high-luminance stimulus (176 cd/m^2) under low-illumination conditions. This central stimulus is the source of the halo perception and other visual disturbances in low ambient lighting conditions, such as experienced in night vision. The size of the stimuli was configured using the radius: 30 pixels for the radius of the central stimulus and 1 pixel for the peripheral one, subtending 0.46 and 0.02 deg, respectively, from observer's position (2.5 m), which was fixed using a chinrest and the forehead. If none of the peripheral stimuli were detected, the radius was increased from 1 to 2 pixels, and so on. A total of 60 peripheral stimuli were randomly presented around the central one distributed along 12 semi-meridians. The task of the patient was to detect (by clicking a mouse button) the peripheral stimuli presented on the monitor, maintaining fixation on the central stimuli. The information was stored and analyzed by the test software, providing a parameter, the visual disturbance index (VDI), which is calculated taking into account non-detected stimuli in relation to the total stimuli presented. This VDI ranged from 0 to 1 for the 1-pixel configuration, where the higher the VDI value, the lower the visual discrimination capacity in dim surroundings and, therefore, the stronger the halos perceived. This parameter is widely described in the literature (Castro et al., 2011; Ortiz et al., 2013a; Castro et al., 2014a; Castro et al., 2014b; Castro et al., 2016). If none of the peripheral stimuli were detected, VDI was 1; the peripheral-stimuli radius was increased from 1 to 2 pixels, and the test was performance again, as in other works (Ortiz et al., 2013a), with the VDI ranging from 1 to 2 for this configuration, and so on.

3.2.5. Intraocular straylight

The intraocular straylight was measured using the C-Quant straylight meter (Oculus GmbH, Wetzlar, Germany) (Figure 7). This device uses the psychophysical compensation comparison method and has been widely applied in clinical studies (de Wit et al., 2006; van den Berg et al., 2009b; Labuz et al., 2017b). The metrics used was the straylight parameter, *s*, which describes the ratio between scattered light and the non-scattered light. The device reports the parameter log(s), which describes the ratio between scattered light and non-scattered light. The higher the log(s), the greater the forward intraocular straylight and, therefore, the stronger the luminous veil over the retinal image. The log(s) parameter increases with age, with values of about 0.90 found for young healthy eyes, 1.03 at 50 years of age, and 1.42 for 80-year-old patients, according to the normal straylight formula (Van den Berg et al., 2007). We took three measurements of straylight for each condition and averaged these. Only values meeting the reliability criterion were considered for the analysis (the expected standard deviation should be less than 0.08).

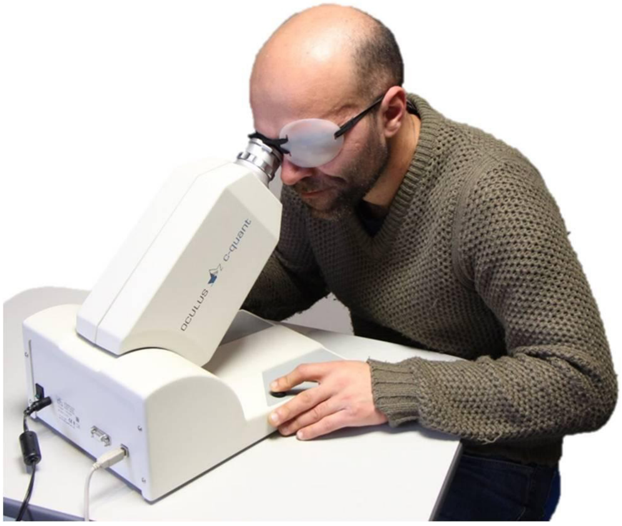


Figure 7. A subject using the C-Quant straylight meter.

3.2.6. Contrast threshold

The contrast threshold (CT) was assessed using the contrast glare tester CGT-1000 (Takagi Seiko Co, Naganoken, Japan). This device measures 12-step contrast thresholds using a central luminous ring as a visual stimulus. To evaluate different spatial frequencies this luminous ring varies in size, subtending angles of 6.3, 4.0, 2.5, 1.6, 1.0, and 0.7 degrees from the observer position (0.35 m), corresponding to the spatial frequencies of 1.0, 1.7, 2.6, 4.2, 6.6, and 10.4 cycles per degree (cpd), respectively. The instrument is described in detail in the literature and it has various applications (Pesudovs, 2007; Ye et al., 2013b; Ortiz et al., 2018b). The CGT-1000 measures the contrast threshold with and without the presence of glare. The glare source used for this comprises 12 white LEDs distributed around the contrast stimulus at 11.8 deg. Three different glare levels are available: low, medium, and high. We used the high glare option (40000 cd/m^2) for the experiment. The CGT-1000 reports the contrast threshold with and without glare for the six spatial frequencies.

3.2.7. Procedures

The visual tests and ocular measurements of our subjects were performed monocularly in a random order, for both eyes, under natural viewing conditions and while wearing each of the Bangerter foils and fog filters. The filters were randomly assigned. Visual acuity (VA) was also included as a visual function in the study, which was evaluated along with visual discrimination capacity under low-illumination conditions, the contrast threshold, and straylight, as well as the ocular measurements (retinal-image quality). Visual acuity was determined in decimal notation using the Pola VistaVision Visual Acuity Chart System (DMD Med Tech, Torino, Italy) at distance (5.5 m). The experiment was split into different sessions to avoid subject fatigue (a session for each filter condition).

3.2.8. Statistical analysis

For the data analysis, we used the SPSS 23.0 software (SPSS Inc., Chicago, IL). We verified the normal distribution of all the visual parameters measured (VA, OSI, Strehl ratio, VDI, log(s), and CT with and without glare) for our healthy young subjects, using the Shapiro-Wilk test (n=14). Then, an ANOVA test for repeated measures using Bonferroni correction was applied to analyze the effects of the different filters (Bangerter foils and fog filters) on the visual parameters measured. For the artificial eye (non-normal distribution), a Friedman test using a two-way ANOVA was run to analyze the OSI and Strehl ratio parameters for the different filters studied. Finally, for the human eyes, we performed several correlations analyses between VDI, OSI and log(s) using the Pearson correlation coefficient (r). Statistical significance was established for a p-value of 0.05 ($p<0.05$).

3.3. RESULTS AND DISCUSSION

The retinal-image quality data for the artificial eye is included in Table 3. The mean values for the objective scatter index (OSI) and the Strehl ratio under natural conditions (no filter) and with the different filters are shown. The OSI was significantly lower under natural conditions than with any of the Bangerter foils ($p<0.001$), although we found no differences when comparing this condition with any of the fog filters ($p=0.999$). The OSI for the artificial eye combined with any of the fog filters was significantly lower than with any of the Bangerter foils ($p<0.001$).

		Artificial eye		Subjects' eyes	
		OSI	Strehl ratio	OSI	Strehl ratio
No filter		0.0 ± 0.0	0.452 ± 0.003	0.5 ± 0.2	0.223 ± 0.057
Bangerter foils	BF_0.8	1.4 ± 0.3	0.073 ± 0.011	4.0 ± 0.4	0.074 ± 0.006
	BF_0.6	2.2 ± 0.6	0.081 ± 0.007	4.9 ± 1.3	0.082 ± 0.009
	BF_0.4	2.9 ± 0.3	0.065 ± 0.006	6.2 ± 1.4	0.064 ± 0.009
	BF_0.3	3.4 ± 0.3	0.064 ± 0.003	8.0 ± 1.2	0.058 ± 0.010
	BF_0.2	7.6 ± 1.0	0.055 ± 0.004	> 10.2	< 0.042
Fog filters	BMP2	0.1 ± 0.0	0.394 ± 0.020	0.8 ± 0.3	0.196 ± 0.051
	Fog_A	0.0 ± 0.0	0.440 ± 0.009	0.6 ± 0.3	0.194 ± 0.032
	Fog_B	0.0 ± 0.0	0.435 ± 0.006	0.6 ± 0.3	0.220 ± 0.048
	Fog_A+B	0.0 ± 0.0	0.432 ± 0.007	0.6 ± 0.3	0.212 ± 0.043
	Fog_1	0.0 ± 0.0	0.427 ± 0.007	0.6 ± 0.3	0.193 ± 0.036

Table 3. Mean Strehl ratio and OSI values for the artificial eye and subject eyes

For the Bangerter foils with the artificial eye, the OSI gradually worsened, on average, from natural conditions to BF_0.2 when following the expected order, with no significant differences being found between BF_0.6 and the other Bangerter foils ($p>0.05$), with exception of BF_0.2 ($p=0.027$). The greatest effect of the induced intraocular scattering was produced with the BF_0.2 foil, where OSI values comparable with a severe cataract were achieved, i.e., scattering levels similar to cataract group NO4 according to the lens opacities classification system (LOCS III) (Artal et al., 2011). The Strehl ratio was significantly lower for the artificial eye with the Bangerter foils compared to natural conditions ($p<0.001$), but also compared to any of the fog filters ($p<0.001$), indicating a deterioration in the retinal-image quality. The highest level of retinal-image deterioration was found in the artificial eye with the BF_0.2 foil, followed by the artificial eye with the BF_0.3, with significant differences between the two conditions ($p<0.001$). For the fog filters, the most important degradation was achieved by the artificial eye with the BPM2 filter, with a significantly lower Strehl ratio than for natural conditions ($p<0.001$), but also lower than the artificial eye wearing the Fog_A ($p=0.007$) and Fog_B ($p=0.036$) filters. The Strehl ratio was also significantly lower for the artificial eye with the Fog_1 filter compared to the unfiltered condition ($p=0.008$), although no significant differences were found when comparing this with any of the other fog filter conditions ($p>0.05$).

Table 3 also includes the mean values for the retinal-image quality parameters (OSI and Strehl ratio) for the subjects' eyes under natural conditions and when wearing each of the Bangerter foils and the fog filters. Considering the OSI and the Strehl ratio, we found a significant deterioration in the retinal-image quality when comparing the subjects' eyes wearing any of the Bangerter foils with the natural conditions ($p<0.001$), excluding the human eyes combined with the BF_0.2 foil, where measurements could not be made due to the extreme deterioration of the retinal image. The OSI was significantly higher for all the fog filters compared to the unfiltered condition ($p<0.05$), except for Fog_1 ($p=0.196$).

We estimated a mean OSI value of greater than 10.2 for human eyes combined with the BF_0.2 foil, since the energy reaching the retina in this case was not high enough to report any results with OQAS for any of the eyes studied. This estimation is justified because the highest OSI value in our experiment was 10.2 for an eye wearing the BF_0.3 foil. For this reason, if measurements were possible, we would expect a significantly higher OSI with the eyes wearing the BF_0.2 foil compared to any of the other conditions studied. This estimation is supported by the results obtained for the artificial eye: the OSI was significantly higher with the BF_0.2 foil than the BF_0.3 foil ($p< 0.001$). According to the cataract classification ranges using the OSI parameter proposed by some authors (Artal et al., 2011) the mean OSI obtained for eyes combined with the BF_0.2 or BF_0.3 foil are comparable with severe cataracts. Furthermore, eyes wearing the BF_0.8, BF_0.6, and BF_0.4 foils are comparable with mature cataracts. For fog filters, only for eyes wearing the BPM2 did the OSI increase to values equating to early-stage cataracts. Some authors have reported that the BPM2 filter induces forward light scattering, providing a good approximation to early-stage cataracts (Cinta Puell and Palomo-Alvarez, 2017; de Wit et al., 2006). The OSI values obtained in our experiment agree with this approximation and it is in line with the cataract classification proposed by Artal et al. (Artal et al., 2011), who reported an early cataract range of $1.0 \leq OSI \leq 3.0$, with a mean OSI for the control group of 0.7 ± 0.3. Our averaged baseline OSI was lower (0.5 ± 0.2) than this and we obtained a mean OSI of 0.8 ± 0.3 for eyes wearing the BPM2 filter, indicating increased intraocular scattering. It should be noted that significant dispersion in OSI values has been reported for patients classified according to the LOCS III classification, depending on the type of cataract (Vilaseca et al., 2012a).

		VA	VDI	log(s)
No filter		1.2 ± 0.1	0.19 ± 0.07	0.85 ± 0.05
Bangerter foils	BF_0.8	0.7 ± 0.1	0.59 ± 0.16	1.15 ± 0.14
	BF_0.6	0.6 ± 0.1	1.39 ± 0.25	1.38 ± 0.07
	BF_0.4	0.4 ± 0.1	1.55 ± 0.18	1.55 ± 0.06
	BF_0.3	0.3 ± 0.1	1.51 ± 0.15	1.53 ± 0.09
	BF_0.2	0.2 ± 0.1	2.59 ± 0.24	1.64 ± 0.05
Fog filters	BPM2	0.9 ± 0.1	0.33 ± 0.15	1.13 ± 0.08
	Fog_A	1.0 ± 0.2	0.32 ± 0.15	1.22 ± 0.15
	Fog_B	1.0 ± 0.2	0.24 ± 0.10	1.26 ± 0.08
	Fog_A+B	1.0 ± 0.1	0.35 ± 0.17	1.48 ± 0.07
	Fog_1	1.0 ± 0.1	0.20 ± 0.09	1.63 ± 0.07

Table 4. Mean monocular values for the different visual functions studied in both eyes of the study subjects

For the Strehl ratio, a significant deterioration was recorded for subjects' eyes combined with any of the Bangerter foils compared to any of the fog-filters (p<0.001). For the BF_0.2 condition, we estimated a mean Strehl ratio of less than 0.042, which corresponds to the lowest value measured in the experiment. We would expect this parameter to be significantly lower than the unfiltered condition, as well as the fog filters, as demonstrated using the artificial eye.

Therefore, Bangerter foils and fog filters resulted in different levels of retinal-image degradation in real eyes (corroborated by an artificial eye) allowing us to analyze visual function under these conditions.

For visual function (Table 4), we found a significantly strong deterioration of all functions with respect to eyes under natural conditions (p<0.001). The visual discrimination capacity under low-illumination conditions significantly and progressively deteriorated for the eyes wearing the Bangerter foils (p<0.001), resulting in a stronger perception of halos and other night-vision disturbances. Statistically significant deteriorations (p<0.001) were found when comparing each foil against the others, except for the comparison of the BF_0.4 and BF_0.3 foils (p=0.476). This deterioration was also evident for the eyes when combined with the BPM2 (p<0.001), Fog_A+B (p=0.001) and Fog_A (p=0.002) filters. Eyes wearing the Fog_1 filter achieved a VDI similar to that recorded under natural conditions.

Figure 8 Night traffic scene with no filter, and as perceived through each filter/foil studied. Each image corresponds to a photograph taken by a commercial camera (Canon EOS 650D) with no filter and using each of the filters/foils analyzed for a fixed configuration of the camera (f/5.6; 1/30 s; ISO 800, 40 mm).

These results are consistent with the night traffic scenes depicted in Figure 8. The night scene viewed through the fog filters shows a predominance of circular halos (with no starburst disturbance), with the strongest halos present for the eyes wearing the Fog_A+B and BPM2 filters, in line with the VDI results (Table 4). The halos were weaker but larger for the Fog_1 filter compared to all the other fog filters, although there was a stronger luminous veil affecting the scene. Night vision disturbances were greater using the Bangerter foils. The night scene viewed through the Bangerter foils shows a specific light disturbance pattern depending on the structure of the foil (Figure 8). As a result, the subject would perceive a combination of visual halos and starbursts affecting a larger area of the scene. A pattern of microbubbles can be appreciated with the Bangerter foils, shown in Figure 9. The bubble density, as well as the shape and size of these bubbles, is related to the image degradation and night-vision disturbances perceived. The BF_0.2 and BF_0.3 foils generate a diffraction pattern compatible with that produced by a square aperture, which is comparable to the shape of the bubbles. The BF_0.8 foil shows the lowest density of bubbles, and their shape is approximately circular. Night vision disturbances induced by the BF_0.8, BF_0.6 and BF_0.4 foils are similar to those reported by some patients after refractive surgery, with a combination of halos and starbursts (Klyce, 2007).

On average, we found a good level of correspondence between the Bangerter foils and the expected visual acuities indicated by the manufacturer, with a standard deviation (SD) of 0.1, except for the BF_0.8 foil with a mean visual acuity of 0.7 ± 0.1 (Table 4). For the Bangerter foils, statistically significant differences were found compared to natural condition but also when comparing foils between them. With the exception of the BMP2 filter, no statistically significant differences were found when comparing the fog filters to each other ($p>0.05$).

The straylight was significantly lower for the eye in natural conditions compared to all the foils and filters ($p<0.001$), indicating a higher amount of forward scattering when any of the foils or filters studied were used. The highest mean log(s) was achieved by the eyes wearing the BF_0.2, followed by the eyes wearing the Fog_1 filter, with no statistical differences between these ($p=0.802$). The straylight increased, on average, in the following order: BPM2, BF_0.8, Fog_A, Fog_B, BF_0.6, Fog_A+B, BF_0.3, BF_0.4, Fog_1, and BF_0.2. Comparing each filter with the subsequent one in this list, statistical significant differences were revealed between Fog_B and BF_0.6 ($p<0.001$), BF_0.6 and Fog_A+B ($p=0.049$), and BF_0.4 and Fog_1 ($p=0.012$). The Fog_1 filter produced less halo effect than the rest of the filters (Table 4), enabling the most stimuli around the main luminous stimulus to be detected in the Halo test, although the amount of straylight was significantly greater than with the rest of the filters (p<0.001), excluding the BF_0.2 foil (p=0.802). These results agree with the night scenes shown in Figure 4, since the shape and size of the streetlights is more precisely defined (softer but larger halos) in the scene corresponding to the Fog_1 filter. In addition, a veil of straylight can be observed affecting the Fog_1 scene, indicating that light from the streetlights is more scattered than with the other fog filters.

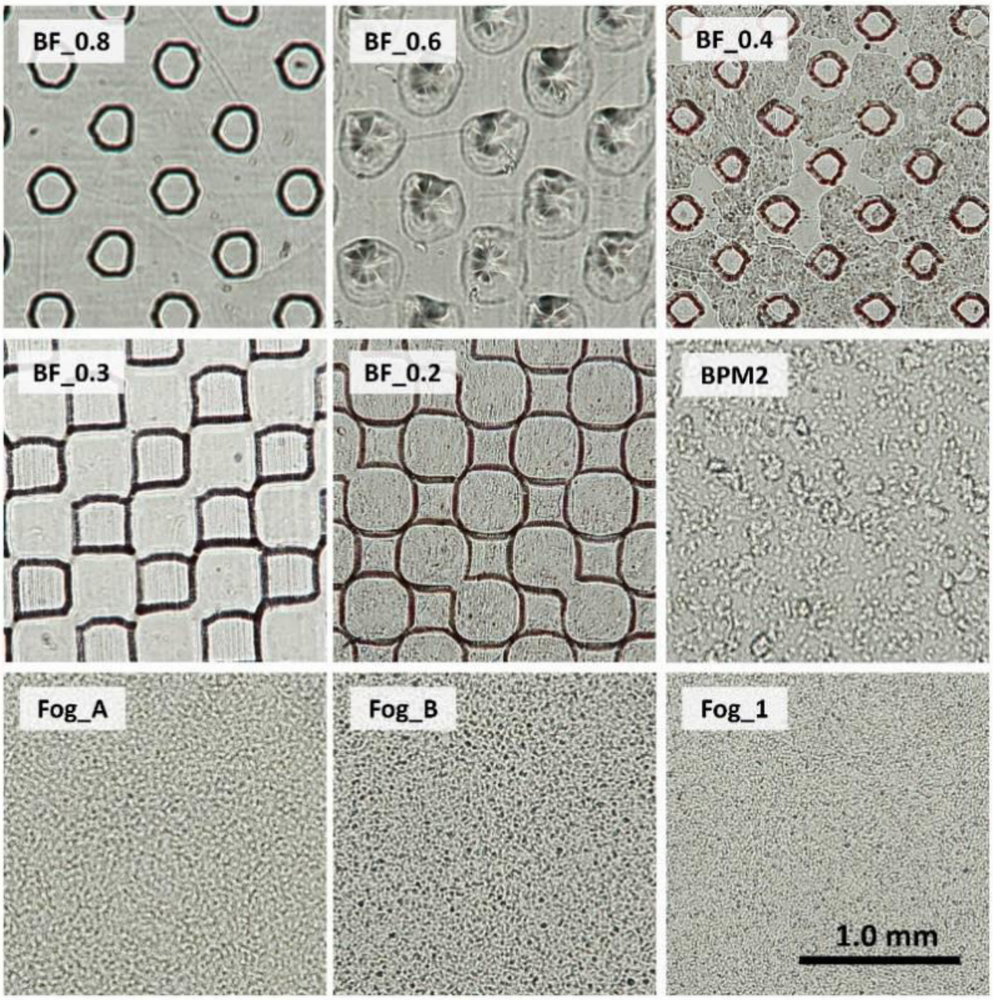


Figure 9 Macro photographs of the patterns in the Bangerter foils and fog filters. using a commercial camera with a 40-mm lens and a 65-mm extension tube. The filters were illuminated using back-lighting (white LED). Each photograph corresponds to an area of 2x2 mm.

The results for the Fog_A+B filter showed a strong halo perception (Figure 8, Table 4) but also provided high straylight values, as can be appreciated in the night scenes (Figure 4). The BPM2 filter provided the lowest straylight values of all the fog filters, although it did give a strong halo effect and higher OSI values.

The corresponding night scenes agree with this assertion, since a softer veil of straylight can be seen than in those observed using the Fog_1 or Fog_A+B filters.

Considering the structure of the fog filters, characterized by their grain size (Figure 9), it can be observed that the smaller the grain size of the filter, the greater the straylight effect and the lower the VDI. The smallest grain corresponds to the Fog_1 filter, for which the highest log(s) and lowest VDI values were reported of any of the fog filters. A similar tendency can be seen for the VDI of the Bangerter foils (see structure of the BF_0.8, BF_0.6, and BF_0.3 foils, whose microbubble density is almost the same).

Our visual acuity and straylight results for the fog filters are in line with those from other studies suggesting that the two parameters are rather independent of one another. This indicates that the visual acuity deterioration in cataracts is caused by aberrations and is not due to straylight (van den Berg, 2017). We have corroborated this independence, since the visual acuity did not vary significantly between fog filters, with the exception of the BPM2 filter. For the Fog_1 filter, the log(s) values were close to those obtained for a grade 2 nuclear cataract (NO2) according to the LOCS III system (Paz Filgueira et al., 2016)

Compared with natural conditions, the contrast threshold was, on average, significantly higher when wearing any of the filters studied ($p<0.001$), with the contrast sensitivity being strongly deteriorated for all spatial frequencies, especially with the Bangerter foils and the Fog_1 and BPM2 filters, as shown in Figure 6. This deterioration was stronger in the presence of glare. In this condition, and while wearing the Bangerter foils (excluding BF_0.8), the participants did not detect the stimulus corresponding to the highest frequency (0.7 deg); they also did not detect this when wearing the Fog_1 filter. In addition, for the BF_0.2 foil with glare, the 1.0 deg stimulus was not detected (Figure 10). The most important differences between the conditions studied in this work were achieved for the high spatial frequencies (low stimulus size); these differences were stronger under glare conditions. In the presence of glare, we found a significant deterioration of the contrast threshold in all the conditions studied compared to natural conditions ($p<0.001$). The results of previous studies have shown the relevance of contrast sensitivity and straylight for characterizing visual function, indicating that a deterioration in these variables can partially predict the performance of a visual task, such as driving (Casares-Lopez et al., 2020a)although when analyzing log(s) values in normal eyes, these authors obtained lower values (maximum mean value of 1.00) than reported in our work. Michael et al. also demonstrated the relevance of straylight when visually assessing drivers, observing that contrast sensitivity correlated well with the self-reported visual quality of drivers (Michael et al., 2009). Other work has demonstrated that straylight (log(s)) is a good visual parameter for predicting simulated driving performance in both young and older people (Casares-Lopez et al., 2020a; Ortiz-Peregrina et al., 2020b).

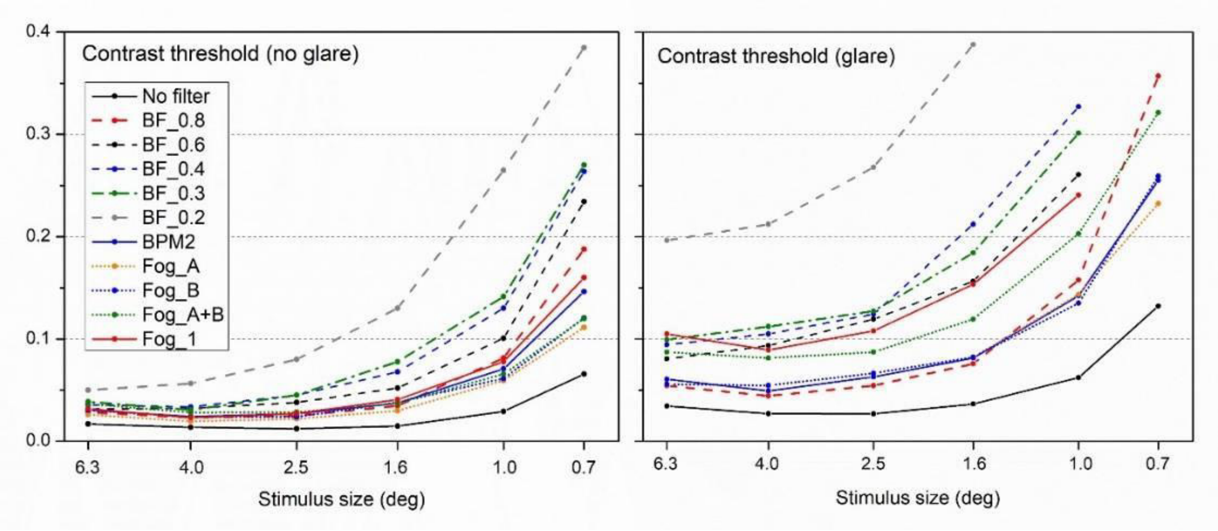


Figure 10. The contrast threshold under normal illumination and under glare conditions as a function of stimulus size.

These results showed that retinal-image degradation negatively affects visual function. Understanding more about the correlation between this image degradation and visual function would be of interest for clinical purposes, especially under low-illumination conditions, where the pupil dilates and the effect of the forward scattering on vision could be stronger. Figure 11 shows the results for the visual disturbance index (VDI) as a function of the scattering index (OSI) for all the conditions studied. Data for the BF_0.2 filter is plotted taking into account the fact that the OSI values in this condition are greater than 10.2 (see region with VDI > 2), as we have previously estimated. The OSI classification for cataracts proposed by Artal et al. has been highlighted in the graph (Artal et al., 2011). This classification is in line with the results reported in others works (Ortiz et al., 2013b; Martinez-Roda et al., 2016a). We found a significant positive correlation (r=0.903, p<0.001) between the parameters analyzed (excluding the BF_0.2 condition). Therefore, the greater the intraocular scattering, the lower the visual discrimination capacity in dim lighting conditions, demonstrating a stronger influence of halos and other visual disturbances. The graphic results (Figure 11) and data in Table 4 reveal a modest tendency towards a lower discrimination capacity with increased cataract severity, in terms of the OSI classification of cataracts. This is corroborated by the results for the BF_0.2 foil with the artificial eye, which presents the highest values of OSI and the highest

VDI values for the observers' eyes. The data for the fog filters graphically locates in a similar area to that for natural conditions, although the highest OSI and VDI values for these filters were achieved with the BPM2 and Fog_A+B. Moreover, the VDI and OSI were, on average, higher for the fog filters than for natural conditions. For the Bangerter foils the VDI and OSI increased significantly, revealing a greater influence of induced scattering and perceived night-vision disturbances.

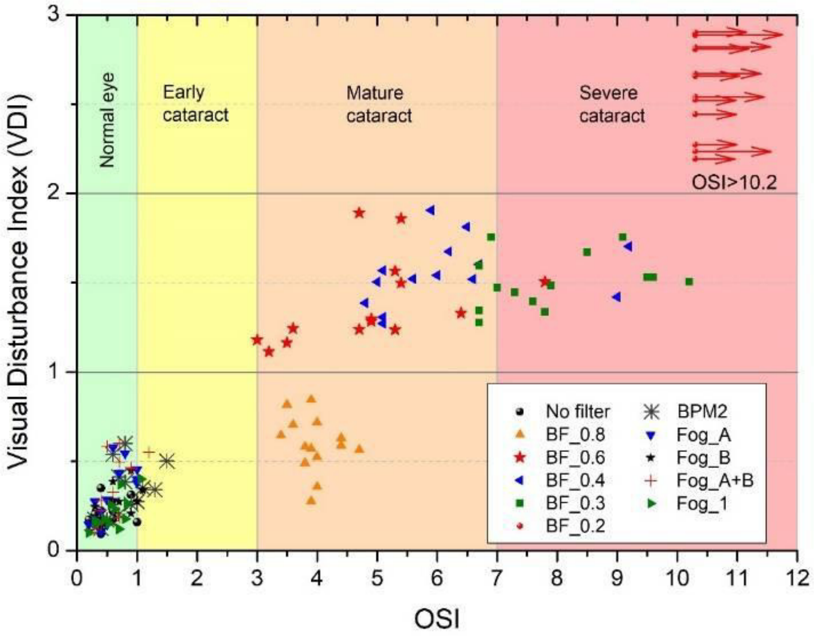


Figure 11. The visual disturbance index (VDI) as a function of the scattering index (OSI) under the conditions studied.

Previous results have reported that a decrease in the Strehl ratio was associated with an increase in halo perception in patients after refractive surgery (Anera et al., 2011), as well as in older patients both with and without cataracts, whose OSI was also analyzed (Ortiz et al., 2013a) Recently, some authors have demonstrated that healthy eyes with a poorer retinal-image quality are related to larger halos (Yao et al., 2020). They analyzed, among other things, the Strehl ratio and OSI, although the range of values analyzed was lower than in our results, and one of the limitations highlighted by the authors was that contrast sensitivity was not evaluated. Furthermore, in these studies, the maximum OSI measured was 2.3 (Ortiz et al., 2013a) a value classified as being similar to an early-stage cataract ($1.0 \leq OSI \leq 3.0$) (Artal et al., 2011; Martinez-Roda et al., 2016b). In our work, we obtained OSI values corresponding to all cataract classification groups, from normal eyes ($OSI < 1$) to severe cataracts ($OSI \geq 7.0$), analyzing a complete range of not only OSI values but also the Strehl ratio and all the visual functions studied.

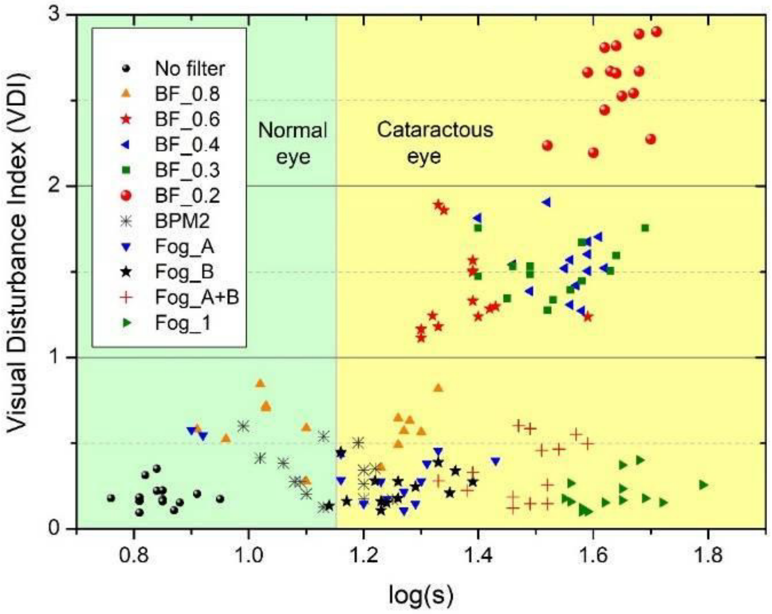


Figure 12. The visual disturbance index (VDI) as a function of the straylight, log(s), under the conditions studied.

On the other hand, Figure 12 shows the influence of log(s) on the visual disturbance index for all the conditions studied. Two ranges of log(s) values are highlighted in the graph: normal eyes and cataractous eyes, according to the log(s) cutoff reported by Martínez-Roda (Martinez-Roda et al., 2016b). We found a significant positive correlation (r=0.866, p<0.001) between the visual disturbance index (VDI) and straylight for the Bangerter foils and natural conditions. However, we found no significant correlation for the fog filters (r=0.033, p=0.767), where only the BPM2 filter showed a significant increase in VDI. Puell et al. reported an ascending correlation between halo size and straylight in healthy eyes with a mean log(s) value of (0.95 ± 0.12), although the authors used a different visual test and metrics to evaluate halo perception (Puell et al., 2014). In our work, we induced different degrees of visual deterioration and we observed a similar tendency for the Bangerter foils and natural conditions, but not for the fog filters. In addition, we analyzed a wider range of straylight values, with average log(s) values ranging from 0.85 to 1.64. Martinez-Roda et al. reported mean log(s) values of 1.49, 1.43, and 1.45 (SDs around 0.3) for nuclear, cortical, and posterior subcapsular cataract groups, respectively, and mean log(s) values of 1.22, 1.43, 1.55, and 1.83 (SDs around 0.2) for grades 1, 2, 3, and 4 of the LOCS III classification, respectively (Martinez-Roda et al., 2016b). Michael et al. found a log(s) value of approximately 1.4 for mild cataracts (Michael et al., 2009). Other authors analyzed straylight in early-stage nuclear and subcapsular cataracts, reporting mean log(s) values of 1.20 and 1.49 for nuclear (NO1 and NO2) and 1.13 and 1.25 for subcapsular (P1 and P2) cataracts, respectively (Paz Filgueira et al., 2016). In our work, we obtained mean log(s) values comparable to LOCS III grades of 1 (Fog_A, Fog_B), 2 (BF_0.6, Fog_A+B), 3 (Fog_A+B, BF_0.4, BF_0.3), and 4 (BF_0.2, Fog_1).

We also obtained a significant ascending correlation (r=0.870, p<0.001) between the log(s) values and the OSI for the Bangerter foils. Again, we found no significant ascending correlation for the fog filters (r=0.081, p=0.464), whereas the straylight did increase significantly for the different fog filter conditions. Some authors have reported a significant correlation between straylight and the OSI in healthy eyes, with log(s) values within a small range (from 0.70 to 1.03 for the straylight, and 0.90 to 1.59 for the OSI) (Iijima et al., 2015). Other authors have demonstrated that log(s) and OSI are good parameters for discriminating between cataractous eyes and healthy eyes for different cataract types according to the LOCS III classification (Martinez-Roda et al., 2016b). However, these authors reported a disagreement between the two parameters, since the OSI is objectively measured with an artificial pupil of 4 mm and using a near-infrared light (780 nm), whereas log(s) is psychophysically measured using white light. Nevertheless, they did observe that the greatest differences between the two parameters were found in eyes with high scattering levels. Some studies have highlighted the limitation of the double-pass technique using an infrared light source, due to the large differences in double-pass images between infrared and green light (van den Berg, 2010, 2011) with the latter (550 nm) being where the human visual sensitivity almost reaches its maximum peak. These differences are principally due to the increased diffuse infrared light from the deeper layers of the retina, mainly from the choroid (van den Berg, 2010), contributing to the total scattered infrared-light in contrast to green light (LopezGil and Artal, 1997). This agrees with the results for log(s) found by other authors analyzing different wavelengths, with the lowest and the highest values of log(s) being obtained for 550 and 800 nm, respectively (Christaras et al., 2016), even though a different method for assessing the log(s) was utilized. These results are in line with other works that have demonstrated an important contribution of diffuse light from the fundus for wavelengths longer than 600nm and small angles (0.5 deg), although such dependence appears weaker for larger angles (Ginis et al., 2013). However, in clinical practice, the use of infrared light contributes to patient comfort during the measurement, since green light typically causes after-images in patients (Vilaseca and Pujol, 2011). Despite this limitation, the double-pass system used in this work has been shown to be a useful device for clinical purposes (Ortiz et al., 2010; Artal et al., 2011; Castro et al., 2011; Ondategui et al., 2012; Xiao et al., 2015; Liu et al., 2019).

The OSI and log(s) represent objective and subjective intraocular forward scattering, respectively. The OSI parameter is calculated by analyzing the light intensity within an annular area of 12 and 20 arc min (“near-angle” scattering) with respect the central peak of the double-pass image (Artal et al., 2011). Likewise, retinal straylight is measured for a visual angle of 5 to 10 deg using the compensation comparison method (Iijima et al., 2015). This angular difference, as well as the structure of the filters, could explain our findings for the fog filters, since the smallest-grain filter (Fog_1) provided the results with the highest log(s) value, i.e., the greatest amount of forward scattering (Table 4, Figure 9) and, therefore, a higher luminous veil over the retinal image. However, for the fog filters, neither the Strehl ratio nor the OSI changed significantly compared to the natural condition, excluding the BPM2. These results reflect the limitation of the commercial double-pass device when measuring the scattering through small-grain (< 40 µm) filters with a uniform grain size, which produced a wider-angle scattering. This also was observed for the Strehl ratio, which was almost the same in the Fog_A, Fog_B, and combination of these (Fog_A+B), as the Strehl ratio includes contributions from intraocular scattering and aberrations working together. Ocular aberrations dominate the central peak of the Point Spread Function (PSF), while intraocular scattering occupies the peripheral part of the PSF (12-20 arcmin for the OSI calculation). These fog filters showed a low level of scattering influence with regard to the OSI parameter, as this double-pass device quantifies the ‘near-angle’ scattering and takes into account a background subtraction due to the contribution of diffuse infrared light from the fundus, making it less sensitive to the forward wide-angle scattering induced by these fog filters. In opposition, the log(s) resulted be more sensitive to forward scattering induced by fog filters, as well as the contrast threshold, especially under glare, as retinal straylight is strongly related to glare sensitivity. The BMP2 filter, which was the largest-grain fog filter (Figure 9) and presented the most irregularity in terms of both grain size and form, provided, on average, the lowest log(s) values, although a significantly higher mean OSI value (and a lower Strehl ratio) was observed. This assertion agrees with the corresponding night scene for the Fog_1 filter (Figure 8), where the shape of the streetlights can be appreciated in detail (not for the BMP2 filter). In this manner, lower OSI values were obtained for the Fog_1 than the BMP2 filter, since, taking into account a small angular distribution, the intensity within the annular area would be lower for the Fog_1 than the BMP2 filter. In the Halo test, the visual discrimination capacity was evaluated within 1 deg of visual angle, as in previous studies (Castro et al., 2014a; Castro et al., 2017). Taking into account our results, there are some conditions where the straylight and glare sensibility increases significantly but the OSI and the halo perception increases only slightly. Again, this is consistent with the night traffic scenes in Figure 8, as well as our results for the fog filters (Table 4): the Fog_1 filter induced smoother and more diffuse halos with a stronger straylight effect on the scene, whereas the OSI did not change significantly compared to the unfiltered condition. Although the Fog_1 filter significantly affected the contrast sensitivity (especially under glare conditions), the study subjects were still able to detect peripheral stimuli in the Halo test. However, halo perception may be greater if the luminance of the peripheral stimuli was low enough, as demonstrated by other authors (Puell et al., 2014). This luminance configuration restricts the VDI-log(s) correlation for the fog filters (Figure 12), due, mainly, to wider-angle scattering compared to the other conditions (BF and BPM2); this creates a veil of straylight over the retinal image, which is better quantified by log(s). Under this condition, we would expect that the visual discrimination capacity would be poorer for the Fog_1 filter, since a higher number of peripheral stimuli would not be detected compared to the BMP2 filter condition.

Some authors have reported that camera filters like those used in this work provide visual acuity and contrast sensitivity values that simulate an early-stage cataract (de Wit et al., 2006). However, in that study, only BPM filters gave the desired cataract straylight values, something that was corroborated when the measurements were performed for only one subject with and without the BPM2 filter, using a research straylight-meter. In other work, Rizzieri et al studied scattered light through three different BPM filters (#1, #3 and #5) and for different wavelengths (405, 532, and 640 nm), finding stronger scattering for the shortest wavelength. They also evaluated vision (VA and CSF) in 10 eyes. Although they did not analyze the BPM2 filter, they found increasing deterioration of visual acuity and contrast sensitivity, especially for the highest frequency, from filters #1 to #5 (Rizzieri et al., 2020). These results are in line with our findings, with the deterioration of visual function for our BPM2 being close to that obtained for BPM3 by Nicola et al.

The Fog_1 filter gave higher log(s) values than the BPM2 filter for straylight angles of less than 10 deg. Other authors have also studied the scattering induced by BPM filters, finding a good correlation level between objective (OSI) and psychophysical evaluations of intraocular light scattering, with similar OSI values to those obtained in this work (Barrionuevo et al., 2010). Our results for a total of 14 eyes, and using a commercial straylight-meter, have also demonstrated that BMP2 is the filter that best simulates an early-stage cataract, taking into account the straylight parameter and OSI values. In addition, we have also found that, using the Fog_A and Fog_B filters, the participants gave log(s) values comparable to an early-stage cataract, although the OSI values corresponded to normal values (non-cataractous eyes). For the Fog_1 filter, we obtained straylight levels comparable to a mature cataract (grades 2-3), although the

OSI and VDI values were within the range of a normal eye, with both of them being slightly higher than in the unfiltered condition.

Puell et al. induced forward light scattering in young eyes using a BPM2 filter, demonstrating a deterioration in low-contrast vision and an increase in halo size (Cinta Puell and Palomo-Alvarez, 2017). However, a circular-disk halo was assumed due to the method used, which only measured halo sections of less than 60 deg. In our study, we analyzed the entire halo, i.e., 360 deg, allowing us to accurately quantify non-circular visual disturbances, such as those seen with some of the Bangerter foils in this work (Figure 8), similar to the starbursts reported by some patients after refractive surgery (Ye et al., 2013a). Pérez et al. analyzed the optical properties of the 0.8, 0.6, 0.4, and 0.3 Bangerter foils (Perez et al., 2010). They found that the structure and optical properties of the 0.6, 0.4, and 0.3 foils were similar, and not necessarily sequential, and only the 0.8 foil was substantially different. Our analysis found a better sequential correspondence between the foils, which were manufactured more recently, although the BF_0.4 and BF_0.3 foils did induce a similar visual function deterioration. It should be highlighted that the orthogonal patterns generated by the periodic structure of the Bangerter foils, especially for foils BF_0.3 and BF_ 0.2 (Figure 8), differ from the starbursts reported by some cataract patients as a consequence of the diffraction caused by the irregularly shaped opacities within the crystalline lens. In this sense, the patterns generated by the BF_0.8 and BF_0.6 foils is closer to those reported by cataract sufferers and patients who have had corneal refractive surgery. Although Bangerter foils are not suitable for simulating cataracts, they do induce scattering levels comparable to different grades of cataracts.

In future work, it would be interesting to analyze other commercial filters, such as holographic diffusers, since the forward scatter profiles are usually provided by manufacturers, as well as to perform the Halo test using different levels of luminance for the peripheral stimuli.

3.4. CONCLUSION

Retinal image quality deterioration negatively affected visual performance for a range of degradation levels. Our results revealed that by inducing forward scattering, the higher the retinal-image degradation, the stronger the visual performance impairment. Increased forward scattering deteriorated the contrast threshold, especially under conditions of glare, as well as the visual discrimination capacity in night-vision conditions and glare sensibility, increasing the perception of halos and other visual disturbances. Bangerter foils induced forward scattering levels equivalent to mature to severe cataracts, and the night-vision disturbances were a combination of halos and starbursts, with these disturbances usually being reported by patients who have undergone ocular surgery or who suffer an ocular pathology. With respect to the OSI parameter, fog filters induced lower levels of forward scattering, and less severe night-vision disturbances, involving a combination of luminous veils and circular halos. The fog filters with the smallest grain size structure induced a very strong straylight effect, although the OSI values were analogous to those recorded under natural conditions. The BPM2 filter induced forward scattering comparable to an early-stage cataract, and the Fog_1 filter produced a very strong luminous veil effect characterized by high log(s) values due to more diffuse straylight distribution on the retinal image, showing the advantage of this measure for evaluating wide-angle scattering induced by small grained fog filters.

The visual discrimination capacity under all the viewing conditions and for a wide range of VDI and OSI values correlated well with the intraocular scattering according to the OSI parameter: the greater the intraocular scattering, the poorer the visual discrimination capacity and the stronger the halo perception and other night-vision disturbances. The Bangerter foils induced a stronger deterioration of the retinal image than the fog filters, mainly due to the structure of the filters.

In this sense, our findings could be of particular interest in the early stages of some ocular pathologies, like cataracts. In these cases, certain visual characteristics remain approximately stable, such as visual acuity, but forward scattering could strongly affect night vision, limiting the performance of some daily tasks, like night driving, or visual tasks in the presence of a glare source. The results of this work could therefore be of interest in clinical and research applications, to help understand how different levels of retinal-image deterioration influence visual performance and the early diagnosis of various ocular pathologies (like cataract), where ocular scattering affects the retinal image. In addition, our results provide a complete evaluation of the different visual disturbances, showing high levels of correlation between night-vision performance and retinal-image quality. This study could also be useful for more accurately determining the visual effects generated by the Bangerter foils when employed in amblyopia treatment for children.

CHAPTER 4

Effect of interocular differences on binocular visual performance after inducing forward scattering (Study 2)

4.1. INTRODUCTION

Assessing binocular visual performance is an important aspect of a visual examination. To evaluate the binocular vision, several studies have investigated the binocular summation for different visual functions (Home, 1978; Blake et al., 1981; Heravian et al., 1990; Eysteinsson et al., 1993; Pardhan, 1996; Baker et al., 2007b; Sabesan et al., 2012b; Yehezkel et al., 2015; Castro et al., 2016) as well as stereopsis (Schor and Heckmann, 1989; Glennerster et al., 1998; Ukwade et al., 2003; Saladin, 2005; Jimenez et al., 2008b; Castro et al., 2010; Westheimer, 2013; Castro et al., 2018). Binocular summation is defined as the superiority of the binocular system with respect to the monocular one in terms of visual function (Blake et al., 1981; Campbell and Green, 1965a), and stereopsis is the ability of the binocular visual system to perceive depth. Binocular visual performance may deteriorate in various ocular pathologies, including cataract (Olson et al., 2017) or age-related macular degeneration (ARMD) (Castro et al., 2011), as well as in ocular disorders such as amblyopia (Holmes and Clarke, 2006), or even after refractive surgery (Anera et al., 2011). Many factors influence binocular performance, for example, interocular differences (differences between the two eyes with regard to a determined monocular visual parameter) as these play an important role in binocular summation, affecting visual performance (Schor and Heckmann, 1989; Saladin, 2005; Jimenez et al., 2007; Castro et al., 2009; Plainis et al., 2013b; Fejes et al., 2014). So et al found that increased interocular differences in visual acuity deteriorate stereopsis (So et al., 2014). Zhao et al suggested that an increment in interocular differences in terms of scatter levels negatively affects stereopsis (Zhao et al., 2018). Jimenez et al reported that interocular differences induced in corneal asphericity after refractive surgery could reduce binocular visual performance even if the subjects became emmetropic after the surgery (Jimenez et al., 2003). Furthermore, in the binocular visual system, sensory ocular dominance (the condition where one eye is preferred to the other for a perceptual visual task related to the sensory visual system (Porac and Coren, 1976) is an important parameter and considered in keratorefractive (Chuck et al., 2018) and cataract surgery (Schwartz and Yatziv, 2015; Olson et al., 2017), in addition to presbyopic correction using monovision (Jain et al., 1996; Fernandes et al., 2018). In monovision, the dominant eye is corrected for distance due to the facility to suppress blur in the non-dominant eye (Jain et al., 1996), creating an interocular difference (anisometropia). A further important phenomenon to consider with regard to how interocular differences affect binocular visual performance is intraocular scattering (forward scattering). Indeed, forward scattering produces a veiling luminance on the retina causing a deterioration in retinal-image quality (Castro et al., 2010), it increases the straylight, and also induces a disability glare, as seen in ocular pathologies such as cataract (Ortiz-Peregrina et al., 2020c) and age-related macular degeneration (ARMD) (Ortiz et al., 2010; Castro et al., 2011). As a result, many visual functions are impaired, including contrast sensitivity (Lorente-Velazquez et al., 2011a; Patterson et al., 2015; Cinta Puell and Palomo-Alvarez, 2017) and night visual discrimination capacity (perception of halos) (Castro et al., 2011). To our knowledge, there is a lack of studies assessing the various degrees of interocular differences in the visual system and the consequent effect of this on binocular summation. In particular, it could be worthwhile evaluating retinal image quality and, more concretely, ocular parameters quantifying forward scattering, such as straylight or others, and their impact on binocular visual performance. This analysis could also be of interest in clinical applications such as refractive surgery (Jimenez et al., 2008a; Anera et al., 2011), monovision (Castro et al., 2016), and ocular pathologies (Ortiz et al., 2010). In this context, various levels of visual degradation and interocular differences can be simulated by using Bangerter foils and fog filters (such as Black Pro Mist 2) (de Wit et al., 2006; Odell et al., 2008; Ikaunieks et al., 2009; Anderson et al., 2009; Perez et al., 2010). Bangerter foils are largely used to treat amblyopia in children, principally penalizing the visual acuity of the non-amblyopic eye (Stewart et al., 2004; Rutstein and Pediatric Eye Dis Investigator, 2010). Additionally, the Black Pro Mist 2 filter has been proved to simulate early cataract by inducing forward scattering (de Wit et al., 2006; Cinta Puell and Palomo-Alvarez, 2017). Taking into consideration the various aforementioned studies, the main assumptions of this study could be that increased interocular differences in some ocular parameters, such as those measuring intraocular scattering and straylight, could have repercussions on visual performance and, also, could reduce binocular summation for certain visual functions and stereopsis. Taking into account these assumptions, the aims of this study were to assess binocular visual performance after deteriorating retinal-image quality by penalizing the dominant eye at different levels. To induce this penalization, we used several Bangerter foils and fog filters to increase monocular forward scattering and, therefore, interocular differences in various ocular characteristics, including intraocular scattering and straylight. We assessed binocular visual performance through binocular summation for various visual functions, such as visual acuity, contrast sensitivity, and visual discrimination capacity (perception of halos), and we also studied stereoacuity at distance. We investigated the effects of various degrees of monocular degradation and interocular differences in several ocular parameters such as intraocular scattering and straylight. Finally, we also analyzed correlations between the binocular summation in visual functions and the interocular differences in ocular parameters, as well as between stereoacuity (at distance) and interocular differences in the various ocular parameters established above.

4.2. METHODS

4.2.1. Subjects

The study was approved by the Human Research Ethics Committee of the University of Granada (921/CEIH/2019). Before participating in the experiment, all participants signed an informed consent form in accordance with the Declaration of Helsinki. A total of 7 young healthy subjects were enrolled in this crossover study (3 females, 4 males) with a mean age of 27.7 ± 6.5 years. The inclusion criteria were decimal visual acuity ≥ 1.0 with best correction for both eyes, normal stereoacuity at distance (40 arcsec or lower), and no pathological conditions or pharmacological treatment that could influence visual performance. A complete eye examination, including objective and subjective refraction, using the endpoint criterion of maximum plus for best visual acuity (in decimal notation), was undertaken for each eye and binocularly at distance (5.5 m) and near (40 cm) under photopic lighting conditions. The mean refractive error (spherical equivalent) was -1.74 ± 2.39 D. Finally, sensory ocular dominance was determined using the line anterior to the best visual acuity and alternating a +1.50 D lens in front of each eye in the binocular condition. The sensory dominant eye was the eye with the positive lens reporting the most blurred vision(Lopes-Ferreira et al., 2013).

4.2.2. Filters

Nine filters were binocularly assessed, with the filter fitted in the dominant eye. Four Bangerter foils (Ryser Optik, St Gallen, Switzerland) corresponding to grades 0.8, 0.6, 0.4, and 0.3 (BF_0.8, BF_0.6, BF_0.4, and BF_0.3) were used to gradually deteriorate the retinal-image quality. We also evaluated the Bangerter foil grade 0.2 but this caused monocular suppression due to the excessive visual difference between the two eyes (Li et al., 2012). Bangerter foils are widely used to treat amblyopia in children (Loudon et al., 2003; Stewart et al., 2004), as well as to optically deteriorate eyesight quality (Odell et al., 2008; Odell et al., 2009; Kingsnorth et al., 2016; Williamson et al., 2021). These foils have a structure of microelements (microbubbles) that produce image distortions (Perez et al., 2010), together with visual acuity and contrast sensitivity degradations (Odell et al., 2008; Rutstein et al., 2011; Williamson et al., 2021). In addition, five fog filters used in photography were assessed: the Black Pro-Mist 2 (Tiffen, Hauppauge, NY); the Fog A and the Fog B filters (HOYA, Kenko Tokina Co., Tokyo, Japan); a combination of the Fog A and Fog B filters (Fog_A+B); and the B+W Fog_1 filter (Schneider, Bad Kreuznach, Germany). The Black Pro-

Mist 2 filter (BPM2) is valid for simulating the effects of early cataract (de Wit et al., 2006) . The Bangerter foils were fixed directly on ophthalmic lenses, with no optical power, previously mounted on identical optical frames, while each of the five fog filters was assembled in Knobloch K-2 shooting glasses (Knobloch Optik GmbH. Karlsruhe, Germany) allowing us to properly fix the lens-holder with the fog filter in front of the eye. All the filters were previously analyzed using the OQAS II device (Optical Quality Analysis System II, Visometrics, Terrasa, Spain), after being fixed onto an artificial eye (TOPCON, spherical refraction -5.5 D).

4.2.3. Visual function and ocular parameters

Visual acuity, contrast sensitivity and stereoacuity

Visual acuity, contrast sensitivity and stereoacuity were evaluated using the Pola VistaVision monitor (DMD MedTech, Villarbasse, Torino, Italy). Visual acuity (VA) was determined in decimal notation, both monocularly and binocularly, using the VistaVision Visual Acuity Chart at a distance of 5.5 m under photopic lighting conditions. Stereopsis was evaluated by means of stereoacuity, which is a binocular parameter quantifying the minimum disparity detected by the subject. It was measured at distance (5.5 m) under photopic lighting conditions using the differentiated stereo D8 polarized test of the Pola VistaVision stereotest, which accurately evaluates the stereopsis (Westheimer, 2013). The contrast sensitivity function (CSF) was evaluated using sinusoidal grids in which the observers had to indicate whether the grid inclined to the right, left, or vertical, with the contrast of these grids being decreased until the impossibility or the mistake in the recognition from the subjects. Eight different spatial frequencies, 0.75, 1.5, 3, 6, 12, and 18 cycles per degree (cpd), were assessed both monocularly and binocularly at 3 m (Casares-Lopez et al., 2020a). The test had a background luminance of 60 cd/m^2 and was performed in mesopic lighting conditions. For each condition, we averaged the contrast sensitivity for all the spatial frequencies. In fact, some authors have shown that binocular summation for this visual function does not vary with the spatial frequencies measured (Ramon Jimenez et al., 2006).

Retinal-image quality

Retinal-image quality was assessed using the OQAS II (Optical Quality Analysis System II, Visometrics, Terrassa, Spain), a double-pass device widely validated in clinical practice (Ortiz et al., 2010; Vilaseca et al., 2012b). Three parameters were measured: the Objective Scatter Index (OSI), the Strehl ratio (SR), and the modulation transfer function cutoff (MTF cutoff). The OSI is an objective parameter quantifying the intraocular scattering which affects the retinal image quality: the higher the OSI value, the greater the intraocular scattering. The Strehl ratio is defined as the ratio between the 2D-MTF area of the eye and the diffraction-limited 2D-MTF area, ranging between 0 to 1: the higher the value, the fewer the ocular aberrations and less scattering. The MTF cutoff represents the spatial frequency corresponding to a theoretical MTF value of 0 (the noise produced by the CCD camera is considered in the calculation of the parameter). We measured and evaluated the retinal-image quality monocularly for both eyes under low ambient illumination, beginning with baseline conditions (without a filter), followed by each Bangerter foil and fog filter in a random order. Three measurements were made and averaged for each experimental condition.

Visual discrimination capacity

The visual discrimination capacity under low-illumination conditions was evaluated using the Halo test (University of Granada, Granada, Spain), based on the Halo v1.0 software. This visual test has been used in clinical applications for ocular pathologies (Castro et al., 2011; Ortiz et al., 2013b) and after refractive surgery (Anera et al., 2011), but also under challenging circumstances to quantify night-vision disturbances (Castro et al., 2014a; Castro et al., 2014b; Ortiz-Peregrina et al., 2020b). The test consists of detecting peripheral luminous stimuli in different positions with respect to a central stimulus with high luminance. This central stimulus is the source of the halo perception and other night-vision disturbances (glare, starbursts, etc.). At the end of the test, a visual disturbance index (VDI) is obtained. This index represents the ratio between non-detected stimuli and all the peripheral stimuli presented to the subject: the higher the VDI the lower the visual discrimination capacity in this illumination condition and, therefore, the stronger the halo perception. Further information on this device can be found elsewhere (Castro et al., 2011; Castro et al., 2014a).

Straylight

Intraocular straylight was assessed under low illumination conditions using the C-Quant straylight meter (Oculus GmbH, Wetzlar, Germany). This device uses a psychophysical compensation comparison method between two test field halves (randomly chosen). As a result, it produces two flickers that differ in modulation depth: one results from straylight and the other is a combination of straylight and compensation light (Franssen et al., 2006). This ocular parameter has been widely used in clinical studies (de Wit et al., 2006; van den Berg et al., 2009a; Labuz et al., 2017a) and introduced into the visual characterization of daily tasks (Michael et al., 2009; Casares-Lopez et al., 2020a). Specifically, the visual parameter log(s) is obtained at the end of the test. The parameter *s* represents the straylight and quantifies the ratio between the scattered and non-scattered light: the higher the value of log(s), the greater the forward intraocular straylight and the consequent increase of the luminous veil over the retinal image. Furthermore, the log(s) parameter increases according to age and in line with the following values given by the normal straylight formula (Van den Berg et al., 2007): 0.90 in young healthy eyes; 1.03 at 50 years of age; and 1.42 at the age of 80. Three measurements were taken to improve the accuracy and reliability of this parameter, and only those values with a standard deviation of less than 0.08 were considered.

4.2.4. Procedures

Each participant took part in different sessions (baseline and one condition for each filter evaluated), none of which were longer than one hour in order to avoid visual fatigue. The order of the visual test measurements was random, to prevent any learning effect. The different sessions (corresponding to the baseline and each filter condition) were also randomized. We measured all the visual functions described above (VA, CSF, stereoacuity, and visual discrimination capacity) both monocular and binocularly, as well as the ocular parameters (OSI, SR, MTF cutoff, and straylight). For the binocular measurements, we evaluated the baseline condition (with no filter), and for the filter condition we inserted the filter in the corresponding lens-holder, checking that it was correctly aligned with the eye. The filter was placed over the sensory dominant eye (Chen et al., 2015). Interocular suppression was checked for all the filters using the Worth-4-dot test.

4.2.5. Interocular differences

Interocular differences (ID) represent the variation between the non-dominant and dominant eye of the subject. We calculated the ID (in absolute values) for all the retinal-image quality parameters (OSI, MTF cutoff, and SR) (Castro et al., 2009; Jimenez et al., 2009) and straylight (log(s)). In this study, we determined the ID between the natural condition (non-dominant eye) and the dominant eye with the associated filter. Finally, an overall interocular difference score (OIDS) was obtained by averaging the z-scores of all the ocular parameters studied (in all the experimental conditions). For all the variables, the more positive the score, the greater the interocular differences. Z-scores have been widely used (Casares-

Lopez et al., 2020a; Ortiz-Peregrina et al., 2020b; Ortiz-Peregrina et al., 2020c) and are a measurement of how many standard deviations an individual value is away from the group mean.

4.2.6. Binocular summation

Binocular summation (BS) assesses the binocular visual performance (Castro et al., 2009; Sabesan et al., 2012b). We evaluated the BS for three visual functions through their corresponding parameters: VA, CSF, and VDI.

The binocular summation for the visual acuity, BS_{VA}, was calculated using Equation (8), dividing the binocular visual acuity, VA_{bin}, by the best monocular eye, VA_{best_mon} (the highest of the two monocular values).

$$BS_{VA} = \frac{VA_{bin}}{VA_{best\_mon}} \tag{8}$$

Similarly, the binocular summation for the CSF, BS_{CSF}, was determined according to Equation (9), dividing the binocular CSF value, CSF_{bin}, by the best monocular value (Castro et al., 2009; Chen et al., 2015; Pardhan, 1997), CSF_{best_mon}.

$$BS_{CSF} = \frac{CSF_{bin}}{CSF_{best\_mon}} \tag{9}$$

Next, the binocular summation for the VDI, BS_{VDI}, was calculated using Equation (10), dividing the lowest monocular value, VDI_{best_mon}, by the binocular VDI value, VDI_{bin}, since the VDI decreases when the discrimination capacity increases (Castro et al., 2016).

$$BS_{VDI} = \frac{VDI_{best\_mon}}{VDI_{bin}} \tag{10}$$

A binocular summation ratio above 1 indicates positive binocular summation, proving the superiority of the binocular system with respect to the monocular one, whereas a value of less than 1 shows the superiority of the best monocular eye measured and the inhibition of the binocular system.

Finally, in line with the OIDS calculation and other studies (Casares-Lopez et al., 2020a; Ortiz-Peregrina et al., 2020b; Ortiz-Peregrina et al., 2020c), an overall binocular summation score (OBSS) was also calculated for the visual functions analyzed (VA, CSF, and VDI), and for all the filter conditions. To do this, we averaged the z-scores of these visual function variables for each filter condition. In this study, the lower the OBSS values, the lower the binocular summation and the lower the binocular visual performance.

4.2.7. Statistical analysis

For the data analysis, we used the SPSS 23.0 software package (SPSS Inc., Chicago, IL). We analyzed the normal distribution of all the parameters (Shapiro-Wilk test). An ANOVA test for repeated measures with Bonferroni correction was used to analyze all the means and variances of all the visual parameters (VA, CSF, stereoacuity, OSI, SR, MTF cutoff, log(s), and VDI) under all the filter conditions. Finally, the Pearson correlation coefficient (r) was used to study the relationship between the overall interocular difference score of the ocular parameters (OIDS) and the overall binocular summation score of the visual functions (OBSS). We also analyzed the relationship between stereoacuity (at distance) and the interocular differences of the ocular parameters (OIDS) using the Pearson correlation coefficient. A statistical significance level of 95% was applied for all the tests ($p<0.05$).

4.3. RESULTS

Table 5 shows the mean binocular values of VA, CSF, VDI, and stereoacuity at distance for the baseline (natural condition) and each filter condition. In all the results, the binocular condition for each filter corresponds to the non-dominant eye without a filter and the corresponding dominant eye wearing the filter. Comparing the baseline to all the filter conditions (Bangerter foils and fog filters), statistically significant deteriorations were found for three visual parameters: VA (Bangerter foils, $p=0.008$ and fog filters, $p=0.038$); CSF (Bangerter foils, $p=0.014$ and fog filters, $p=0.049$); and stereoacuity (Bangerter foils, $p=0.011$ and fog filters, $p=0.032$). Comparing each condition to the worst result (with BF_0.3), we found significant VA impairments in all the conditions ($p=0.026$) except for BF_0.6 ($p=0.095$) and BF_0.4 ($p=0.163$). Similarly, for stereoacuity at distance, we also found impairments for all the conditions ($p=0.024$) except for BF_0.4 ($p=0.325$). Stereoacuity at distance is therefore strongly impaired with the Bangerter foils and less so with the fog filters. For the CSF, the worst situation was determined using the

BF_0.4 foil, which showed a significant difference compared with BF_0.8 (p=0.044) and all the fog filter conditions (p<0.05).

For the VDI, the best results were found binocularly in the baseline and Fog_1 condition, but statistically significant differences were observed with the BF_0.6 (p=0.024), BF_0.4 (p=0.014), and Fog_B (p=0.019) conditions. Subsequently, marginally significant differences were seen with BF_0.8 (p=0.057), but not BF_0.3 (p=0.093). The worst VDI result was for BF_0.4, resulting in significant impairment compared to the baseline (p=0.014), and all the fog conditions (p=0.023), but not compared to the other Bangerter foils (p>0.05). Finally, in all the visual parameters, no statistically significant differences were seen when comparing between the fog filters (p>0.05). Therefore, for these different visual parameters measured, significant deteriorations were revealed in all the filter conditions with respect to the baseline, with the worst condition being with the Bangerter foils.

		VA	CSF	Stereoacuity (arcsec)	VDI
Baseline	(no filter)	1.3 ± 0.1	166 ± 4	20 ± 8	0.13 ± 0.04
Bangerter foils	BF_0.8	1.1 ± 0.1	139 ± 14	83 ± 90	0.18 ± 0.09
	BF_0.6	1.1 ± 0.1	137 ± 17	104 ± 64	0.23 ± 0.12
	BF_0.4	1.1 ± 0.2	127 ± 17	180 ± 98	0.26 ± 0.13
	BF_0.3	0.9 ± 0.2	134 ± 24	231 ± 122	0.19 ± 0.09
Fog filters	BPM2	1.2 ± 0.2	146 ± 14	36 ± 24	0.15 ± 0.08
	Fog_A	1.2 ± 0.2	144 ± 18	36 ± 17	0.13 ± 0.03
	Fog_B	1.2 ± 0.2	143 ± 15	39 ± 21	0.16 ± 0.05
	Fog_A+B	1.2 ± 0.2	155 ± 12	34 ± 19	0.13 ± 0.05
	Fog_1	1.2 ± 0.2	154 ± 8	39 ± 22	0.13 ± 0.04

Table 5. Mean values (standard deviations included) of the binocular visual functions: visual acuity (VA), averaged contrast sensitivity function (CSF), stereoacuity at distance, and visual disturbance index (VDI) for the different Bangerter foils and fog filters used.

Figure 13 shows the mean OSI values for the artificial eye and the subjects' eyes. Mean interocular differences for the OSI parameter are also included. For the artificial eye, the mean OSI values for the baseline and all the fog filters were equal to 0 with the exception of BPM2 (OSI = 0.1). For the baseline condition, statistically significant differences were obtained when compared to all the Bangerter foils (p<0.05). These foils gradually increased the OSI value, the worst condition being found with the BF_0.3 foil. Statistically significant impairments were obtained when comparing the Bangerter foils between each other (p<0.05) with the exception of the comparison between BF_0.8 and BF_0.6 (p=0.197). For the subjects' eyes, statistically significant differences were found between the baseline and all the Bangerter foils (p<0.05) but not with the fog filters (p>0.05). For the Bangerter foils, the OSI impaired progressively from BF_0.8 to BF_0.3 (p<0.05) with statistical differences between BF_0.8 and BF_0.6 (p=0.044).

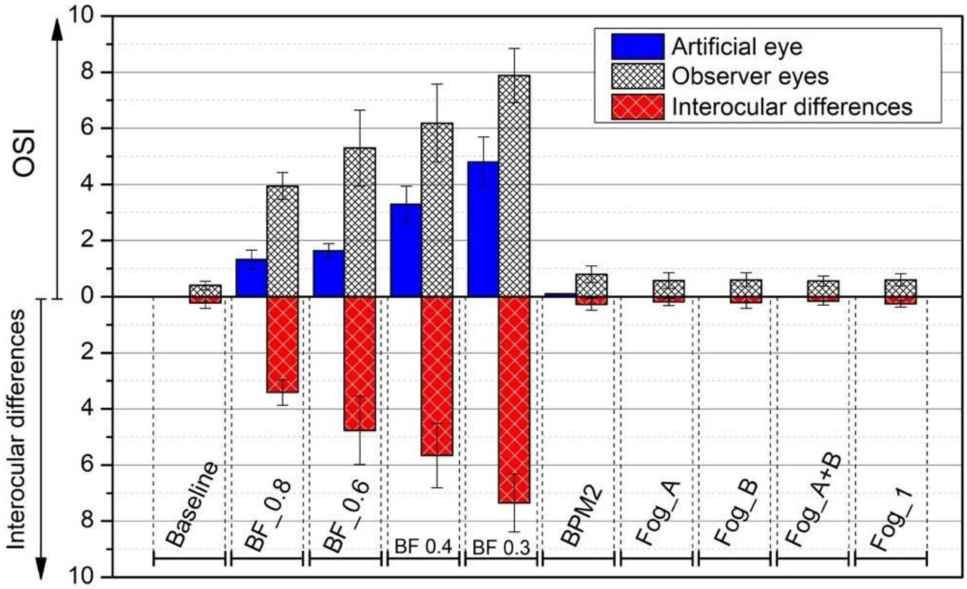


Figure 13. Mean OSI values for the artificial eye and observer eyes for all the experimental conditions (baseline and the different filter conditions). The mean interocular differences for the OSI in observer eyes are also included.

Table 6 shows the mean values of the interocular differences for the three retinal-image quality parameters (SR, MTF cutoff, and OSI) and straylight (log(s)). For the SR and MTF cutoff, significant increases were observed between the natural condition and all the Bangerter foil conditions (p<0.05), but not when comparing baseline to any of the fog filter condition (p>0.05). In fact, on average, decreases in the interocular differences for the SR and MTF cutoff were found for all the fog filters respect to the no filter condition (except for Fog_1 in the MTF cutoff), where the most significant difference was obtained when comparing the BPM2 filter and the natural condition for the MTF cutoff parameter (p=0.009). In addition, for the SR and MTF cutoff, the interocular differences increased progressively from the BF_0.6 to the BF_0.3 foils (p<0.05) but not between the BF_0.8 and the BF_0.6 foils (p>0.05). Similarly, for the OSI, significant increases in the interocular differences were found with all the Bangerter foils measured with respect to the baseline (p<0.001). On average, the interocular differences of the OSI increased progressively from BF_0.8 to BF_0.3 but not statistically between BF_0.6 and BF_0.4 (p=0.203). On the other hand, the interocular differences for the BF_0.3 condition were significantly higher than the other filter conditions for the OSI (p<0.001), being marginally significant when compared to BF_0.4 (for MTF cutoff, p=0.051 and for OSI, p=0.053). For the interocular differences in all the fog filter conditions, no statistical increases were observed compared to the baseline condition (p=0.384). In terms of straylight, the interocular differences of log(s) were significantly lower for the baseline condition compared to the Bangerter foils and fog filter conditions (p=0.003). Ultimately, compared to the baseline (no filter) condition, the interocular differences for the three retinal-image quality parameters increased significantly for the Bangerter foil conditions but not with the fog filters.

		Interocular differences			
		SR	MTF cutoff (cpd)	OSI	log(s)
Baseline	(no filter)	0.08 ± 0.05	10.9 ± 5.9	0.21 ± 0.20	0.06 ± 0.04
Bangerter foils	BF_0.8	0.15 ± 0.07	29.4 ± 10.2	3.41 ± 0.46	0.37 ± 0.16
	BF_0.6	0.14 ± 0.06	28.2 ± 8.5	4.77 ± 1.22	0.54 ± 0.05
	BF_0.4	0.16 ± 0.07	31.4 ± 8.2	5.66 ± 1.14	0.72 ± 0.06
	BF_0.3	0.17 ± 0.07	33.2 ± 9.1	7.35 ± 1.04	0.69 ± 0.10
Fog filters	BPM2	0.04 ± 0.04	4.1 ± 4.2	0.27 ± 0.21	0.29 ± 0.08
	Fog_A	0.06 ± 0.05	6.0 ± 4.2	0.19 ± 0.13	0.35 ± 0.15
	Fog_B	0.07 ± 0.05	8.0 ± 4.7	0.21 ± 0.21	0.43 ± 0.09
	Fog_A+B	0.05 ± 0.05	6.5 ± 6.7	0.16 ± 0.14	0.64 ± 0.12
	Fog_1	0.06 ± 0.05	11.3 ± 6.4	0.25 ± 0.12	0.79 ± 0.13

Table 6 Mean values of the interocular differences for the ocular parameters analyzed: Strehl ratio (SR), modulation transfer function cutoff (MTF cutoff), objective scatter index (OSI), and straylight (log(s)) under the experimental conditions studied (baseline and wearing each of the Bangerter foils and fog filters).

Table 7 indicates the mean values of the binocular summation (BS) for the visual functions VA, CSF, and VDI under the different experimental conditions measured. For VA, positive binocular summation ($BS_{VA} > 1$) was obtained for the baseline and the fog filter conditions, except with BPM2. The highest mean value was obtained for the BS in the baseline condition which was statistically higher than all the filter conditions (p<0.05). Binocular summations for VA decreased gradually from BF_0.8 to BF_0.3, revealing inhibition of this parameter with all the Bangerter foils ($BS_{VA} < 1$) (Apkarian et al., 1981). Considering the CSF, positive binocular summations ($1 < BS_{CSF} < 2$) were found for all the conditions except with BF_0.4, the greatest being for the baseline condition (1.31±0.20). In fact, statistically significant differences were observed for the baseline binocular summation compared to all the Bangerter foil conditions (p=0.020), but also compared to the fog filters (p=0.025). On the other hand, statistically significant differences were observed between the lowest binocular summation value (BF_0.4) and BF_0.8 (p=0.034), as well as all the fog filters (p=0.044). Finally, for the CSF, binocular summation gradually decreased with the Bangerter foils (except for BF_0.3). Similarly, for the VDI, binocular summation gradually deteriorated with the Bangerter foils (except for BF_0.3) with respect to the baseline, being below 1 for the BF_0.6 and BF_0.4 conditions. Nonetheless, improvements in the binocular summation were found for the fog filters except for Fog_B, the highest value of BS being recorded when wearing the Fog_1 filter. As a result, the binocular summation declined with the Bangerter foil conditions, mainly affecting the VA and VDI values. In contrast, the binocular summation values for the fog filters remained above 1. In fact, fog filters placed on the dominant eye did not lower the binocular summation, providing even better binocular summation results for the VDI compared with the natural condition (except for Fog_B).

		Binocular summation		
		VA	**CSF**	**VDI**
Baseline	(no filter)	1.14 ± 0.07	1.31 ± 0.20	1.33 ± 0.43
Bangerter Foils	BF 0.8	0.97 ± 0.07	1.09 ± 0.19	1.17 ± 0.50
	BF 0.6	0.96 ± 0.13	1.08 ± 0.22	0.90 ± 0.25
	BF 0.4	0.91 ± 0.13	1.00 ± 0.21	0.81 ± 0.26
	BF 0.3	0.80 ± 0.11	1.05 ± 0.23	1.14 ± 0.51
Fog Filters	BPM2	1.00 ± 0.09	1.15 ± 0.20	1.33 ± 0.36
	Fog A	1.05 ± 0.13	1.13± 0.17	1.46 ± 0.36
	Fog B	1.05 ± 0.10	1.11 ± 0.15	1.15 ± 0.12
	Fog A+B	1.02 ± 0.13	1.22 ± 0.21	1.44 ± 0.31
	Fog 1	1.03 ± 0.06	1.22 ± 0.23	1.47 ± 0.25

Table 7. Mean binocular summation values for the visual parameters: visual acuity (VA), contrast sensitivity function (CSF), and visual disturbance index (VDI) for the different Bangerter foils and fog filters used. “No filter” represents the natural condition.

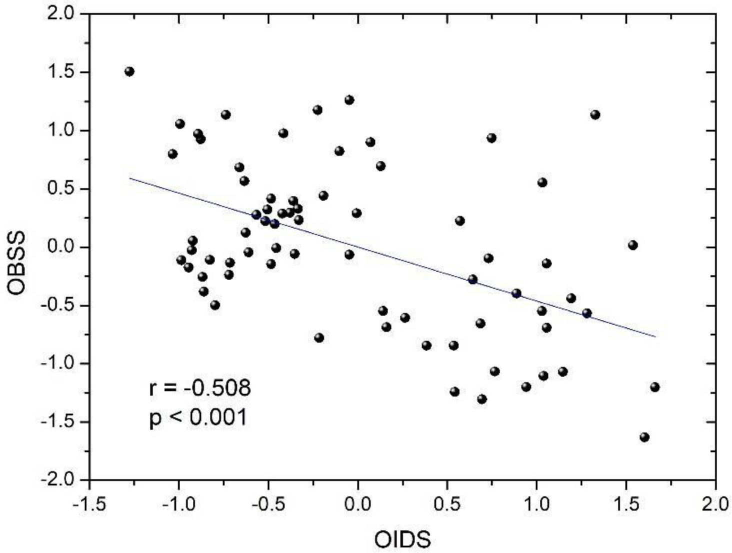


Figure 14 The overall interocular difference score (OIDS) of the ocular parameters analyzed as a function of the overall binocular summation score (OBSS) of the visual function.

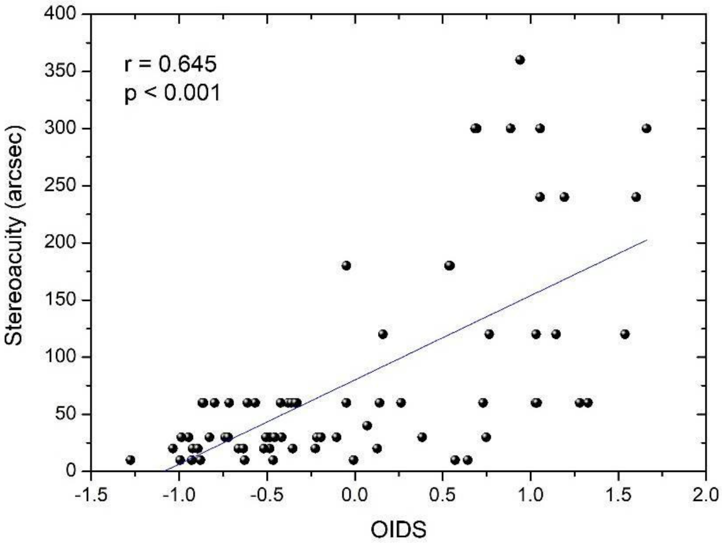


Figure 15. The overall interocular difference score (OIDS) of the ocular parameters analyzed as a function of stereoacuity at distance (arc sec).

Figure 14 shows the relationship calculated between the overall interocular difference score (OIDS) and the overall binocular summation score (OBSS). A statistically significant negative correlation was found between the OIDS and OBSS (r= -0.508, p<0.001), revealing that the higher the OIDS, the lower the OBSS.

As a result, the higher the interocular differences for the ocular parameters analyzed, the lower the binocular summation for the visual functions measured and, therefore, a stronger deterioration in binocular visual performance.

Figure 15 shows the relationship calculated between the overall ocular parameter interocular difference score (OIDS) and stereoacuity (SA) at distance. A statistically significant positive correlation ($r= 0.645$, $p<0.001$) was found between OIDS and SA, revealing that the higher the OIDS, the greater the stereoacuity at distance. As a result, the greater the interocular differences for the ocular parameters analyzed, the higher the stereoacuity values and, therefore, a stronger degradation in stereoscopic perception at distance.

4.4. DISCUSSION

This study allowed an overview of binocular visual performance under natural conditions and after simulating various degrees of degradation on the dominant eye with Bangerter foils and fog filters. Taking into consideration all the visual functions analyzed binocularly, VA, CSF, and stereoacuity showed statistically significant deterioration with all the filters with respect to the baseline condition. For visual discrimination capacity in low ambient illumination, using the VDI metrics, we found statistically significant degradation mainly with the Bangerter foils (BF_0.6, BF_0.4). For the ocular parameters (MTF cutoff, Strehl ratio, OSI, and log(s)), the increase in scattered light through the ocular media (induced by the filters) deteriorated the optical quality of the eye, resulting in a worsened retinal-image (Castro-Torres et al., 2021). Thereafter, the binocular summations were calculated for the visual functions mentioned above (VA, SC and VDI), indicating a lower binocular summation ($BS < 1$) only for Bangerter foils in some cases: in terms of visual acuity (BF_0.8, BF_0.6, BF_0.4 and BF_0.3), and VDI (BF_0.6 and BF_0.4). We found that, on average, the binocular summation for VA and the CSF diminished with respect to the baseline condition for all the filter conditions. Binocular summations for the VDI deteriorated with the Bangerter foils and the Fog_B filter. Thus, the interocular differences also increased with all the Bangerter foils for the ocular parameters (MTF cutoff, Strehl ratio, and OSI) but also for straylight (log(s)) compared with the baseline condition. For the OSI and log(s) parameters, the higher the deterioration degree of the Bangerter foil, the higher the interocular differences. For the fog filters, no increments in the interocular differences were revealed for the ocular parameters measured with the OQAS (MTF cutoff, Strehl ratio, and OSI), in contrast to the straylight (log(s)) assessed using the C-Quant device, where important increases in the interocular differences were observed with these filters. Several important points concerning these two devices have to be taken into consideration. Firstly, the discrepancy could be due to methodological differences. In fact, the OQAS double-pass device provides objective measurements whereas the C-Quant device supplies the log(s) parameter through the compensation comparison method. Secondly, the OSI measured with the OQAS analyzes the double-pass retinal image of a point source of light corresponding to the ratio between the light intensity (annular area of 12 and 20 arc min) and the intensity reaching the central peak (1 arc min) (Artal et al., 2011). Similarly, retinal straylight measured with the C-Quant device is for a visual angle of 5 to 10 degrees. Thirdly, another important difference could involve the light used in these two devices: the OQAS uses a near-infrared light (λ=780 nm), while the C-Quant has a white light source, for which visual sensitivity peaks at 550 nm (Chapter 3). For the OQAS device, the infrared light is more suitable for estimating the measurements of retinal image quality than visible light, providing additional comfort for the patient (Jimenez et al., 2008c; Castro et al., 2011; Martinez-Roda et al., 2016b). Even if there are certain limitations with the OQAS device, such as the artifact created by infrared light diffusion in the choroid causing diffusion and back reflection (Martinez-Roda et al., 2016b), the OQAS device has been proved to be an accurate and reliable device in several clinical applications (Jimenez et al., 2008c; Ortiz et al., 2010; Castro et al., 2011; Ondategui et al., 2012; Xiao et al., 2015; Liu et al., 2019). The last point is that the structure of the fog filters could also influence the results: the Fog_1 filter is the smallest-grained fog filter and the BPM2, the largest-grained (Chapter 3). Uniform small grain filters produce "wider-angle" scattering. For low-moderate levels of induced forward scattering, the OQAS device quantifies the "near angle" scattering, and with the contribution of its infrared light reaching the background, this device is limited and less sensitive to the forward wide-angle scattering due to the small grain size (<40 µm) and uniformity induced by fog filters (Chapter 3). In contrast, the log(s) parameter measured with the C-Quant device is more sensitive to the wide-angle forward scattering of the fog filters, inducing higher interocular differences (Chapter 3).

Conversely, statistically significant correlations were found when comparing the interocular differences in the ocular parameters (OIDS) to the binocular summations for the visual functions (OBSS) and stereoacuity. In fact, the higher the interocular differences for the ocular parameters (OSI, RS, MTF cutoff, and log(s)), the lower the binocular summation for the different visual parameters investigated (VA, CSF, and VDI). Stereoacuity at distance correlated with all the interocular differences measured, demonstrating deteriorated stereoacuity with the increased interocular differences for the ocular parameters cited above. Our study is in line with that of Zhao et al who found deteriorated stereoacuity induced by three different scatter filters placed binocularly in front of the eyes (Pro Mist 1/2, Pro Mist 1, Pro Mist 2) suggesting a mutual influence between the increment of interocular differences in scatter levels and the deterioration of the stereoacuity (Zhao et al., 2018). Similarly, we evaluated the influence of scattering on stereopsis, although we provided additional information to objectively characterize the scatter level induced (by means of ocular parameters such as OSI, RS, MTF cutoff, and log(s)) and for a wide range of interocular differences induced by Bangerter filters (higher interocular differences than the BPM filters) and fog filters. In addition, we calculated that binocular visual performance deteriorated with increased interocular differences in the various visual parameters of retinal image quality (RS, MTF cutoff, and OSI) and straylight (log(s)). As a result, the increased forward scattering induced by the filters on the dominant eye produced greater interocular differences that deteriorated overall binocular visual performance.

On the other hand, increments in the interocular differences (considering retinal image quality and straylight parameters) simulated by the different filters deteriorated the binocular summation of the visual functions measured (VA, CS and VDI). Moreover, inhibitions in these binocular summations (BS < 1) were found for all the Bangerter foil conditions for visual acuity and Bangerter foils 0.6 and 0.4 for the binocular discrimination capacity (VDI), resulting in no improvement in the binocular visual system. In fact, the perception and binocular-discrimination capacity proved to be worse than in the monocular state, indicating a major limitation when inhibiting the binocular summation inherent to our visual system. In contrast, for Bangerter foil 0.3, the binocular summation for the contrast sensitivity function and VDI were above 1, but this was not the case for the binocular summation for visual acuity. This may be explained by two main reasons: the time spent on the visual task, and the ensuing monocular partial suppression. Indeed, in this study, the visual tasks that took the longest were the assessment of contrast sensitivity function (CSF) and visual disturbances (VDI), compared to the short time taken for measuring visual acuity. Another important point is that Bangerter foil 0.3 caused greater forward scattering than all the other filters measured. So, even if the interocular suppression was verified and controlled by the Worth-4-dot test, we could not exclude the possibility that monocular partial suppression in the eye wearing the Bangerter foil 0.3 occurs in the lengthier visual tasks (Li et al., 2012). Another explanation could be the adaptation of the binocular system to important retinal blur, as caused by Bangerter foil 0.3. In fact, Plainis et al found that binocular summation inducing different degrees of defocus (retinal blur) increased, suggesting the activation of a larger population of neurons under binocular stimulation (Plainis et al., 2011). In contrast, when the image quality of the two eyes is dissimilar (as occurs with the Bangerter foils), stereopsis is significantly reduced (Jimenez et al., 2008a). Our study agrees with these findings. Our results corroborate the fact that binocular summation for different visual functions decreases with interocular difference increments in ocular parameters. Castro et al found that the greater the interocular differences in the Strehl ratio, the more reduction there is in the binocular summation of the contrast sensitivity function, showing high degrees of correlation ($r^2 = 0.80$) between them (Castro et al., 2009). An important factor to take into account is that the test sensitivity used for evaluating the CSF in that study was higher than in the present study, which could affect any comparison of the results. Likewise, Jimenez et al found descending correlations between the binocular summation for the CSF and the interocular differences in the higher-order aberrations, demonstrating deteriorated visual performance with such interocular differences (Jimenez et al., 2008b). In fact, Sabesan et al confirmed higher values in the binocular summation correcting the higher-order aberrations, and determining neural adaptation with ocular aberrations (Sabesan et al., 2012b). Moreover, Nitta et al found that subjects with a strong imbalance in sensory dominance had lower binocular summations for contrast sensitivity and confirmed that ocular dominance is crucial for clinical applications, such as the monovision used for correcting presbyopia (Nitta et al., 2007). This is in line with our study where, taking into account several levels of interocular differences (induced by the different filters) in various ocular parameters (OSI, RS, MTF cutoff and log(s)), we found consequent decreases in the binocular summation of the different visual parameters investigated (VA, CSF and VDI). The different simulated deteriorations, particularly with the Bangerter foils and the BPM2, confirmed that the increment in straylight and intraocular scattering deteriorate the binocular summation for the visual functions investigated (visual acuity, contrast sensitivity, and visual discrimination capacity). Our results could be useful for clinical practice, where the visual evolution in several ocular pathologies (Jimenez et al., 2008c; Ortiz et al., 2010; Castro et al., 2011; Vilaseca et al., 2012b) (keratitis, ARMD, cataracts, etc.) and ocular surgeries (Ramon Jimenez et al., 2006; Anera et al., 2011; Ondategui et al., 2012; Xiao et al., 2015; Liu et al., 2019) (myopic photorefractive keratectomy, LASIK, cataract surge, etc.) occur in one eye first, contributing to the interocular differences (due to the forward scattering), producing binocular imbalance and a successive decrease in binocular visual performance. In particular, the visual parameters measured in this study are inherent in patients with cataract where, due to lens opacity, straylight and intraocular scattering increase, disrupting the retinal-image quality and binocular visual performance (Anderson et al., 2009; Barrionuevo et al., 2010; Artal et al., 2011; Hwang et al., 2018b).

A second important point from this research is the relationship between the increased interocular differences in the ocular parameters measured and the consequent worsening in stereoacuity at distance:

the greater the interocular differences, the stronger the impairment in stereoacuity at distance and, therefore, the poorer the stereoscopic perception. Stereoscopic perception allows the visual system to see the surrounding environment in depth, being paramount in important complex task such as driving (Casares-Lopez et al., 2020a; Ortiz-Peregrina et al., 2020c). We produced a large range of interocular differences, primarily using the Bangerter foils and the BPM2 filter on the dominant eye. These relationships are in line with other studies. Li et al reported that penalizing the dominant eye with a Bangerter foil reliably decreased stereoscopic depth perception for all filter strengths (Li et al., 2012). Zhao et al suggested that the higher the scatter levels induced by BPM filters, the greater the deterioration in stereopsis (Zhao et al., 2018). Also, Perez et al when characterizing the Bangerter foils, disclosed the important degradation in stereoacuity they caused (Perez et al., 2010). Odell et al also selected Bangerter foils to induce monocular blur, and confirmed a consequent progressive degradation of stereoacuity thresholds (Odell et al., 2009).

The interocular differences in blur sensitivity appear to be a useful factor in the further grading of eye dominance, binocular viewing conditions being modified by increases in these interocular differences (Johansson et al., 2015). Considering the possible correlations between interocular differences and binocular visual performance, Castro et al analyzed the interocular differences in optical quality (higher order aberrations and Strehl ratio) on the maximum disparity (the total range of stereoscopic perception) under mesopic conditions, and also found an important correlation between these interocular differences and the increment in stereothresholds (Castro et al., 2017). Others studies (Jimenez et al., 2008b; Jimenez et al., 2009) have confirmed that the higher the interocular differences, the less effective the binocular summation and the lower the maximum disparity. An important impact caused by interocular difference increases after LASIK surgery was investigated by Jimenez et al where they found that increments in interocular differences in corneal asphericity significantly deteriorated stereopsis (Jimenez et al., 2008a). However, in our study, the wide range of filters used (Bangerter foils and fog filters) made it possible to produce and simulate different levels of stereoacuity deterioration, providing a better understanding of stereopsis as well as binocular visual performance. Furthermore, the wide range of interocular differences in the ocular parameters analyzed has been correlated firstly with the overall binocular summation of several visual functions and, in a second phase, with the stereopsis.

4.5. CONCLUSION

The different impairments applied to the dominant eye revealed an important factor in the study of binocular visual performance. The increase of forward scattering, induced mainly by the Bangerter foils and the fog filter BPM2 on the dominant eye, produced greater interocular differences which jeopardized overall binocular visual performance. Specifically, this caused a decrease in the binocular summation (VA, CSF and VDI) and deteriorated stereopsis (at distance), which correlated with the increased interocular difference. In this regard, our study reveals that it is necessary to avoid considerable interocular differences in ocular parameters such as optical quality (OSI), intraocular scattering, and straylight (log(s)) to preserve adequate binocular visual performance (stereopsis and binocular summation).

This study could therefore be very useful in terms of specific binocular visual aspects like refractive surgery or ocular pathologies when these first affect one eye, as well as in presbyopia (monovision contact lenses), amblyopia, and emmetropization techniques which could impact complex visual task like driving.

CHAPTER 5

Pupil Size Effect on Binocular Summation for Visual Acuity and Light Disturbance (Study 3)

5.1. INTRODUCTION

Normal binocular vision depends on a considerable number of optical and neural parameters (Campbell and Green, 1965b). One of these important parameters is the pupil size. Human visual performance depends strongly on pupil size, particularly in highly aberrated eyes (Sabesan et al., 2012a; Bonaque-Gonzalez et al., 2016; Xu et al., 2018), but also in healthy eyes (Thibos et al., 2002; Mello et al., 2012; Plainis et al., 2013a). Several physiological factors affect pupil size (Castro et al., 2016): namely age (Ross et al., 1985), environmental lighting or visual complexity task among others (Frisen and Lindblom, 1988; Medina et al., 2003). Pupil size also changes between monocular and binocular vision conditions being generally lower under binocular vision for the same age and environmental light. In healthy people, binocular sensitivity has been found to be higher compared to monocular sensitivity, due to binocular summation (Tyler and Apkarian, 1985; Heravian et al., 1990; Eysteinsson et al., 1993). Nevertheless, an opposite effect (decrease) in the binocular summation was disclosed after corneal refractive surgery procedures such as LASIK (Ramon Jimenez et al., 2006; Villa et al., 2009). Binocular summation refers to the superiority of binocular vision performance over monocular vision performance (Campbell and Green, 1965a; Blake et al., 1981; Tyler and Apkarian, 1985; Heravian et al., 1990). If this factor is above 1, there is a positive effect and, therefore, an enhancement on binocular condition compared to the best monocular condition (Castro et al., 2016; Heravian et al., 1990). Moreover, this factor positively affects several metrics of visual performance, including improvements in visual acuity, contrast sensitivity (Blake et al., 1981; Frisen and Lindblom, 1988; Weeber et al., 2010; Plainis et al., 2011; Sabesan et al., 2012a; Schwarz et al., 2014) and reduction of light disturbance (Fernandes et al., 2018). Light disturbance is a photic phenomenon which includes some specific visual disturbances generally described as glare disability, starburst and halos. Regarding these visual disturbances, glare disability cause a reduction of visual performance due to a glare source. Starburst and halos can alter and degrade the object shape or size. Also, halos can occur with or without starbursts (radial or regular scattering of light from a point source) (Fan-Paul et al., 2002). In fact, light disturbance is an important aspect to take into account in multifocal contact lenses (Fernandes et al., 2018) and intraocular implantation of multifocal intraocular lenses (Brito et al., 2015; Escandon-Garcia et al., 2018). Sabesan et al observed that binocular summation increases as contrast decreases under the conditions of high stimulus energies and low noise (Sabesan et al., 2012a). Plainis et al investigated the effect of binocular summation in eyes undergoing deterioration of retinal image quality with defocus and showed that binocular vision ameliorates the effect of retinal blur on spatial visual performance (Plainis et al., 2011). Escandon-Garcia et al observed a 30%

improvement in light disturbance under binocular compared to monocular conditions after multifocal IOL implantation. However, they did not control for potential changes of pupil size between binocular and monocular conditions (Escandon-Garcia et al., 2018). Therefore, it is unclear whether this improvement reflects a neural summation factor or simply an optical effect due to the improvement in optical quality by pupil reduction under binocular vision conditions.

With this in mind, the present study has been designed to assess the impact of pupil size on high and low contrast visual acuity and light disturbance in young healthy eyes undergoing different spherical and cylindrical defocus levels. Moreover, this study has investigated the binocular summation under different pupil size conditions, fixed for monocular and binocular conditions in order to eliminate the potential effect of pupil constriction. The study has also evaluated the potential correlations between visual acuity (psychophysical parameter) and light disturbance index (a psychophysical parameter which quantifies the light disturbance). This information will be used as reference for designing future studies involving these two metrics of visual performance. For example, it can be used in subjects with ocular disease, or in those undergoing optical or surgical visual correction. Also, it might be helpful for comparing with objective parameters.

5.2. METHODS

5.2.1. Subjects

The inclusion criteria to participate on this crossover study were: only emmetropic or myopic subjects with a spherical refraction less than |-3.0 D| and an astigmatism less than |-1.0 D|, monocular and binocular visual acuity ≤ 0.00 (logMAR notation) with binocular visual acuity better than monocular ones, no ocular pathology or surgery and no pharmacological treatment which could affect their vision or pupil response. Additionally, all the subjects had to have a pupil diameter superior to five millimeters under the illumination conditions for the visual acuity optotype (illuminance of 170.3 ± 3.9 lx) and LDA device allowing to standardize an artificial pupil size of 5 mm and 3 mm using artificial diaphragms (5 mm and 3 mm). A full eye examination for each participant was conducted including objective and subjective refraction using the endpoint criterion of maximum plus for the best visual acuity. A subjective refraction exam was checked (best monocular VA for each eye and corresponding best binocular balance). The probability is 81 percent that the study will detect a difference at a one-sided 0.05 significance level, if the true difference between treatments is 0.050 units. This is based on the assumption that the standard deviation of the difference in the response variables is 0.07. The pupil diameter was measured with the NeurOptics pupilometer (NeurOptics VIP TM- 200, California) which has been proved to have very good repeatability and high safety (Schallenberg et al., 2010). Pupil size was measured while the subject was looking at the light disturbance analyser central light to ensure we measured the smaller pupil as a reference under this and the remaining test conditions (i.e. visual acuity measurement).

Two positive spherical defocus levels (+1.5 and +3.0 D) and two positive cylindrical defocus levels (+1.5 and +3.0 D at 90°) were used to induce a controlled degradation of the retinal image. The order of defocus was random for the two pupil size conditions (5 and 3mm) using artificial diaphragms at 12 mm from the corneal vertex on a trial frame.

To obtain all the data, two sessions of one hour were required. In the first session, all the low (LCDVA) and high (HCDVA) contrast distance visual acuity measurements were determined for the baseline and all the defocus levels (spherical and cylindrical) with the two pupil size conditions (5 and 3 mm). In the second session, all the LDI (Light Disturbance Index) values were obtained for the two pupil size conditions and the different levels of defocus (spherical and cylindrical). Patients wore the best spectacle correction on trial frame for the evaluation distance. Following the Declaration of Helsinki, all patients were informed and carry out about the purpose of the study and all methods. All the subjects had the opportunity to clarify their doubts and sign an informed consent form before being enrolled in the study. So, the informed consent was obtained for all the participants. The study protocol was reviewed and approved by the Ethics Subcommittee for Life and Health Sciences of the University of Minho.

5.2.2. High and low contrast visual acuity at distance

The best visual acuity with the ETDRS logMAR charts at a distance of 4 meters under Low Contrast (LCDVA, 10%) and High Contrast (HCDVA, 100%) conditions was measured. The measurements were obtained under a photopic illumination room condition: the luminance was 86.23±1.75 cd/m^2 and the illuminance was 170.27±3.86 lx, measured with the Minolta LS-110 Luminance meter and the Minolta T10A Illuminance meter, respectively. The different defocus levels and pupil diameters were presented in a random order to avoid any learning effect to influence the results.

5.2.3. Light Disturbance

In order to quantify light disturbance, the halometer called Light Disturbance Analyzer (LDA, CEORLab, University of Minho, Braga, Portugal) was used. This device analyses the size and shape of the halo surrounding a bright light under dim illumination conditions. In practical terms, the test consisted of identifying a peripheral stimulus (small whit LED ref. HSMW-CL25 from Avago Technologies, San Jose, California) around a central LED stimulus (white LED ref. HLMP-CW47-RU000 from Agilent Technologies, Inc., Berkshire, United Kingdom) under low-illumination conditions. The central LED is responsible for creating the glare condition while the surrounding LEDs are used as threshold discriminators at different positions and angular distances of the visual field (Linhares et al., 2013). So, the peripheral LEDs are only used to indicate the limits of the size of the halo caused by the central LED stimulus. This methodology is similar to other visual tests to quantify night-vision disturbances which use luminous stimuli around a central high-luminance stimulus to determine the halo size (Castro et al., 2014a; Castro et al., 2014b). The peripheral LEDs of the LDA are distributed in twenty-four semi-meridians with an angular separation of 15 degree. According to Linhares et al during the test, the central LED had a maximum luminance of 2800 cd/m^2, and 6 cd/m^2 for the surrounding LEDs, and, therefore, the central high-luminance LED is responsible of the halo perception and, maintaining constant the luminance of the stimuli, the detection of the surrounding LEDs would allow to determine the shape and size of the halo or visual disturbance (Linhares et al., 2013). The peripheral stimuli were presented randomly around the central LED from the inner to the outer part of the field at random times from 250 ms to 750 ms. The subject was placed at a distance of two meters from the centre of the central LED stimulus under low illumination surrounding conditions (illuminance of 0.91±0.02 lx) and had to continuously maintain the fixation on the central LED stimulus. The subject has to press the mouse control button each time the peripheral stimulus is seen and the system presents the next semi-meridian. Three evaluations are performed in each semi-meridian before the instrument calculates the mean limit of the light distortion. If the standard deviation (SD) of the three evaluations in each semi-meridian is superior to 20%, the device automatically repeats the measurements in those semi-meridians until reach a SD inferior to 20%. At the end of the test, a map of the size of the light disturbance (halo) is obtained (Ferreira-Neves et al., 2015). One main parameter evaluates the degree of these dysphotopsias: the Light Disturbance Index (LDI). The LDI is calculated as the ratio of the area of the points missed by the subject and the total area explored: the higher the LDI, the higher the light disturbance induced by the central source of light and the lower the ability to discriminate surrounding small stimuli. This parameter is commonly used as a percentage in studies using the same device (Ferreira-Neves et al., 2015; Brito et al., 2015; Macedo-de-Araujo et al., 2016; Escandon-Garcia et al., 2018; Fernandes et al., 2018), but it can be also expressed as the angular size of the halo radius from the observer position (in degrees or arc min). A LDI value of 100% corresponds to detect no one of the peripheral stimuli showed to the observer (a halo radius of 137.4 arc min from the observer position). In this work the LDI is expressed as the radius of the halo from the observer position (in arc min).

5.2.4. Binocular Summation

The binocular summation characterizes the binocular visual performance (Pardhan, 1996; Castro et al., 2009; Sabesan et al., 2012a). For the low and high contrast visual acuity, the binocular summation ratio BS_{VA} was calculated using the Equation (11), dividing the binocular visual acuity, VA_{bin}, by the best monocular one, VA_{best_mon} (the higher of the two monocular values). For this calculation, decimal visual acuities were used, which were previously obtained from the logMAR VA values.

$$BS_{VA} = \frac{VA_{bin}}{VA_{best\_mon}} \qquad (11)$$

Regarding the light disturbance parameter LDI (Light Disturbance index), the discrimination capacity increases when the LDI decreases. Therefore, the LDI binocular summation, BS_{LDI}, was calculated using the Equation (12), dividing the lowest monocular value, LDI_{best_mon}, by the binocular LDI value LDI_{bin}. This calculation is in accordance with other authors who used an index comparable to the LDI (Castro et al., 2016).

$$BS_{LDI} = \frac{LDI_{best\_mon}}{LDI_{bin}} \qquad (12)$$

A binocular summation ratio superior to 1 indicates a positive binocular summation showing that the vision is better binocularly compared to monocular conditions.

5.2.5. Statistical procedures

The statistical analysis was performed using SPSS 23.0 (SPSS Inc., Chicago, IL) for Windows. The normality was checked using the Shapiro-Wilk test (n=15). In case of normality of the data, repeated measures ANOVA with Bonferroni correction were used for LDCVA and HDVCA parameters and the multiple comparisons between baseline, defocus and pupil sizes. Alike, in case of non-parametric nature of the data, Friedman test with post-hoc correction was used for LDI and the multiple comparisons between baseline, defocus and pupil sizes. Degree of freedom shortened in DF. It was also compared between monocular and binocular conditions with same defocus and pupil size. Therefore, in case of normality, Pearson correlation (Pearson R) was performed to find the relationship between defocus and visual acuity. Spearman Correlation (Spearman R) was made to find the relationship between light disturbance parameters and visual acuity (LCDVA and HCDVA). Differences were considered statistically significant when the p value was lower than 0.05.

5.3. RESULTS

5.3.1. Subjects

A total of 15 young subjects (11 females, 4 males) were recruited in this crossover study. The mean age was 28.5±7.7 years. Table 8 shows mean refractive error of the participants as well as their mean pupil size under natural conditions but also under the LDA measurement conditions.

n=15		Mean values (SD)
Natural pupil diameter (mm)		6.1±0.6
Natural pupil diameter under LDA measurements conditions (mm)		5.65±0.30
Refraction	Sphere (D)	-0.42±0.82
	Cylinder (D)	-0.25±0.43

Table 8. Average pupil diameter (mm) and refraction (D) of the subjects enrolled in the study. Standard deviation (SD) included.

5.3.2. High and low contrast visual acuity at distance

Figure 16 shows the mean values of the low contrast distance visual acuity (LCDVA), monocularly and binocularly, under the different defocus conditions studied and for the two pupil diameters (3 and 5mm). No significant differences between right and left eye in all measuring conditions (spherical and cylindrical defocus, and pupil sizes) were found ($F_{1,14}$=2.047, p=0.174). Nevertheless, all the LCDVA monocular parameters were found to be significantly higher than the binocular ones in all measuring conditions ($F_{2,14}$= 7.447, p=0.016), which indicates a poorer visual performance in logMAR scale. The pupil size of 5mm showed a statistically significant deterioration compared to the pupil size 3mm in all measuring conditions ($F_{1,14}$= 6.395, p=0.024). With spherical defocus and pupil size of 5mm condition, a statistically significant deterioration in LCDVA was found proportionally with the amount of defocus. Monocularly, for each amount of +1.5 D, a deterioration of 0.53 logMAR in LCDVA (Pearson R=0.999, p<0.001) was disclosed ($F_{1,14}$= 100.870, p<0.001). Similarly, in the binocular condition (pupil size of 5mm), a statistically significant deterioration ($F_{1,14}$= 104.334, p<0.001) was showed with increasing the spherical defocus (Pearson R=0.999, p<0.001). A deterioration of 0.41 logMAR on average between baseline and spherical defocus of +1.5 D and a mean value deterioration of 0.47 logMAR between spherical defocus of +1.5 and +3.0 D were found. Likewise, with the pupil size of 3mm, monocularly and binocularly, a statistical significant deterioration ($F_{1,14}$= 106,258, p<0.001) was found proportionally with the amount of defocus (Pearson R=0.999, p<0.001).

Similarly, results showed a statistically significant deterioration of LCDVA inducing cylindrical defocus compared with baseline measurements. Monocularly, for the pupil size of 5mm, a degradation was shown for cylindrical defocus condition, with a minimum mean difference of 0.32 logMAR between baseline and +1.5 D ($F_{1,14}$= 151.874, p<0.001) and of 0.33 logMAR between +1.5 D and +3.0 D of cylindrical defocus ($F_{1,14}$= 122.263 p<0.001). Similar results were obtained binocularly: an average LCDVA deterioration for cylindrical defocus condition with a mean difference of 0.31 logMAR between baseline and +1.5 D ($F_{1,14}$= 157.118, p<0.001) and a mean difference of 0.28 logMAR between +1.5 D and +3.0 D of cylindrical defocus ($F_{1,14}$= 115.126, p<0.001). As a result, a strong correlation was demonstrated between cylindrical defocus and LCDVA (Pearson R=0.999, p<0.001) for the 5mm pupil.

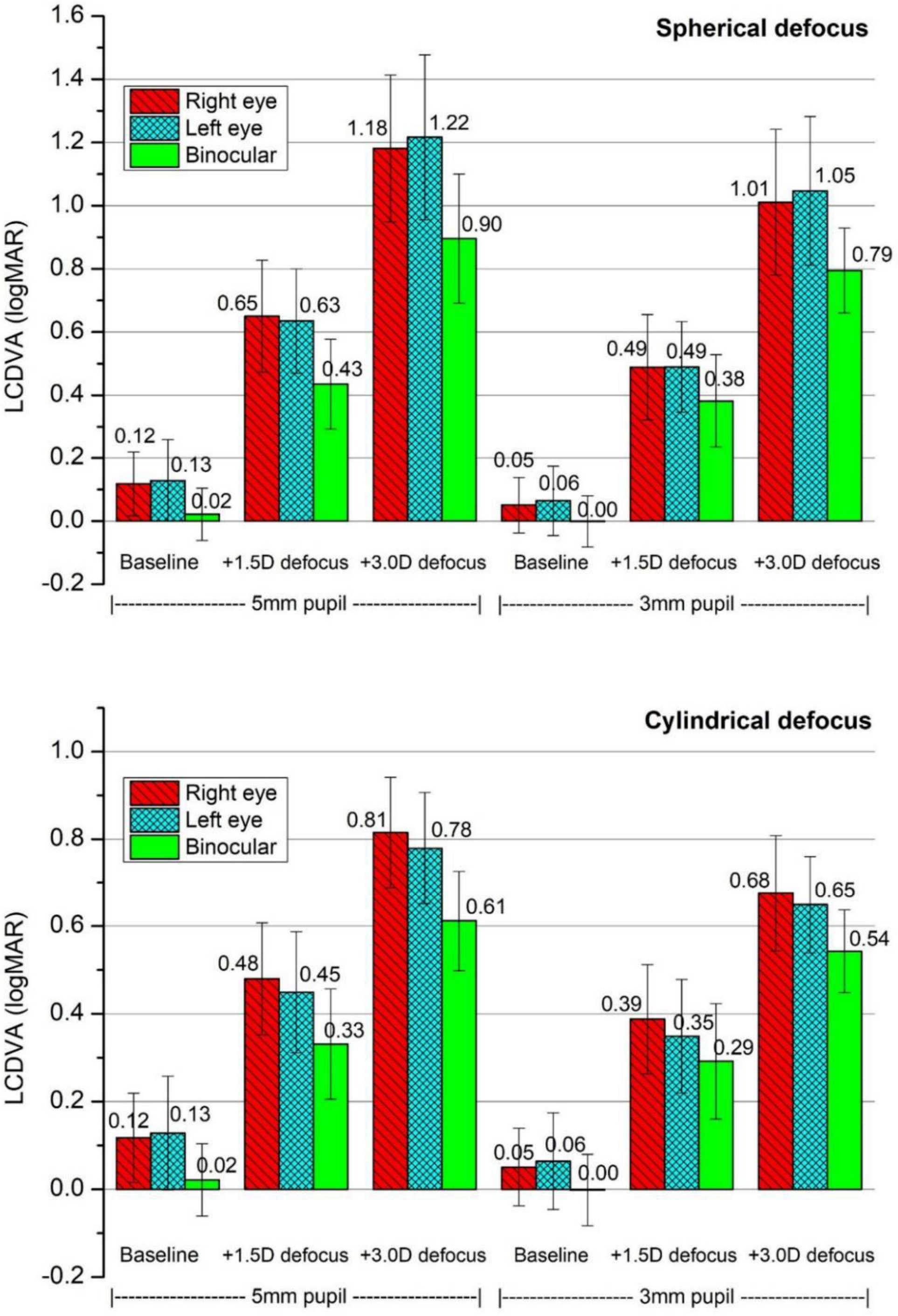
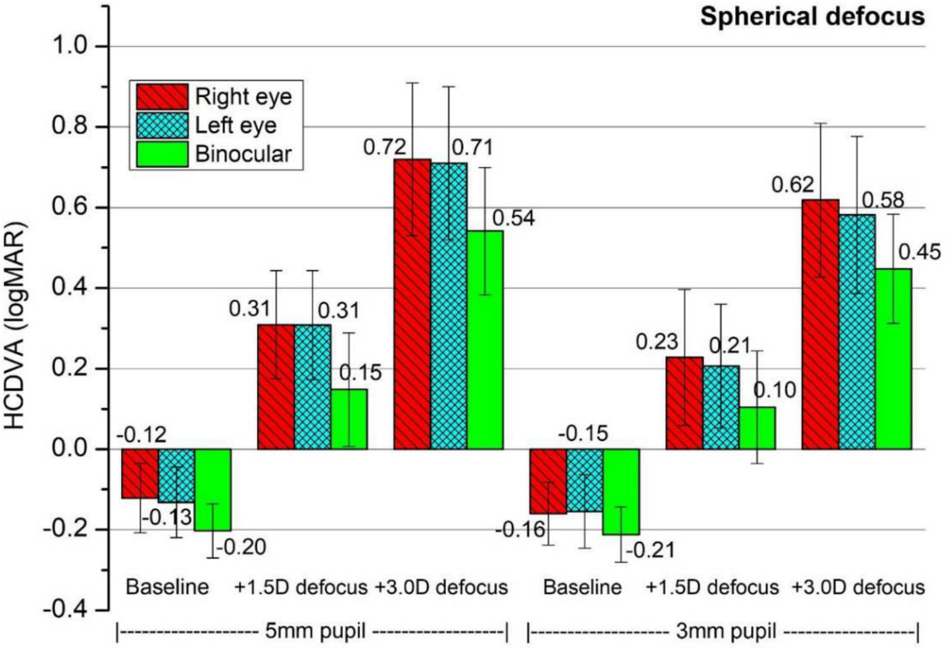


Figure 16. Average and standard deviation values of logMAR distance visual acuity for low contrast (LCDVA) under spherical (+1.5 and +3.0 D) and cylindrical defocus (+1.5 D at 90° and +3.0 D at 90°) for 3 and 5 millimeters (mm) pupil size condition (n=15). Baseline data (no defocus) are included.



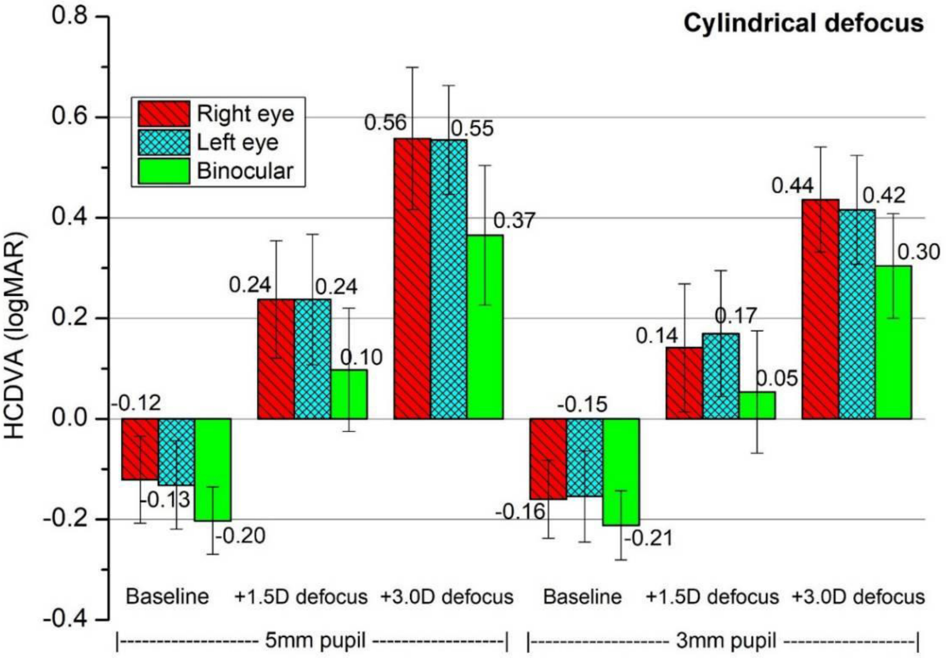


Figure 17. Average and standard deviation values of logMAR distance visual acuity for high contrast (HCDVA) under spherical (+1.5 D and +3.0 D) and cylindrical defocus (+1.5 D at 90° and +3.0 D at 90°) for 3 and 5 millimeters (mm) pupil size condition (n=15). Baseline data (no defocus) are included.

For the pupil size of 3 mm, significant deteriorations of LCDVA were also found for cylindrical defocus condition under monocular viewing for both comparisons: a mean difference of 0.29 logMAR between baseline and +1.5 D ($F_{1,14}$= 163.348 p<0.001) and a mean difference of 0.30 logMAR between +1.5 D and +3.0 D of cylindrical defocus ($F_{1,14}$= 128.986, p<0.001). Binocularly, average LCDVA deteriorations were also obtained, with a mean difference of 0.29 logMAR between baseline and +1.5 D ($F_{1,14}$= 128.986, p<0.001) and a mean difference of 0.25 logMAR between +1.5 and +3.0 D of cylindrical defocus ($F_{1,14}$= 115.126, p<0.001). As a result, a strong correlation was demonstrated between cylindrical defocus and LCDVA (Pearson R=0.999, p<0.001) for the smallest pupil.

Figure 17 shows mean values for the high contrast distance visual acuity (HCDVA) under the different conditions tested (spherical and cylindrical defocus and the two pupil sizes of 3 and 5 mm). No statistically significant differences were found between left and right eye in all the conditions ($F_{1,14}$= 1.158, p=0.300). A strong correlation between defocus (spherical and cylindrical) and HCDVA (Pearson R=0.999) was demonstrated. All the binocular mean values were statistically (repeated measures ANOVA and Bonferroni correction) better than the monocular ones ($F_{2,14}$= 11.227, p=0.005). Comparing pupil size between 5mm and 3mm, the HCDVA mean values were significantly better for the 3mm pupil ($F_{1,14}$=5.651 p=0.032 for baseline; $F_{1,14}$=12.171 p=0.004 for spherical conditions; and $F_{1,14}$=6.271, p=0.025 for cylindrical defocus) in all the conditions (spherical and cylindrical defocus, monocularly and binocularly) except binocularly for the baseline where differences were no significant (-0.20 ± 0.07 logMAR for the 5mm and -0.21 ± 0.07 logMAR for the 3 mm pupil; $F_{1,14}$=2.318 p=0.150).

Table 9 shows the mean values of the binocular summation for the visual acuities studied (LCDVA and HCDVA). In all conditions, a positive binocular summation was obtained: the mean binocular summation was higher than 1, highlighting the superiority of binocular visual system compared with the monocular one. Therefore, the binocular visual acuity was better than the best monocular one. As a result, for the LCDVA, it was observed that the binocular summation increased significantly under larger pupil size in all the conditions ($F_{1,14}$=6.444, p=0.024 for baseline; $F_{1,14}$= 31.818, p=0.001 for spherical and $F_{1,14}$=11.477, p=0.004 for cylindrical) and, furthermore, higher level of spherical defocus was achieved.

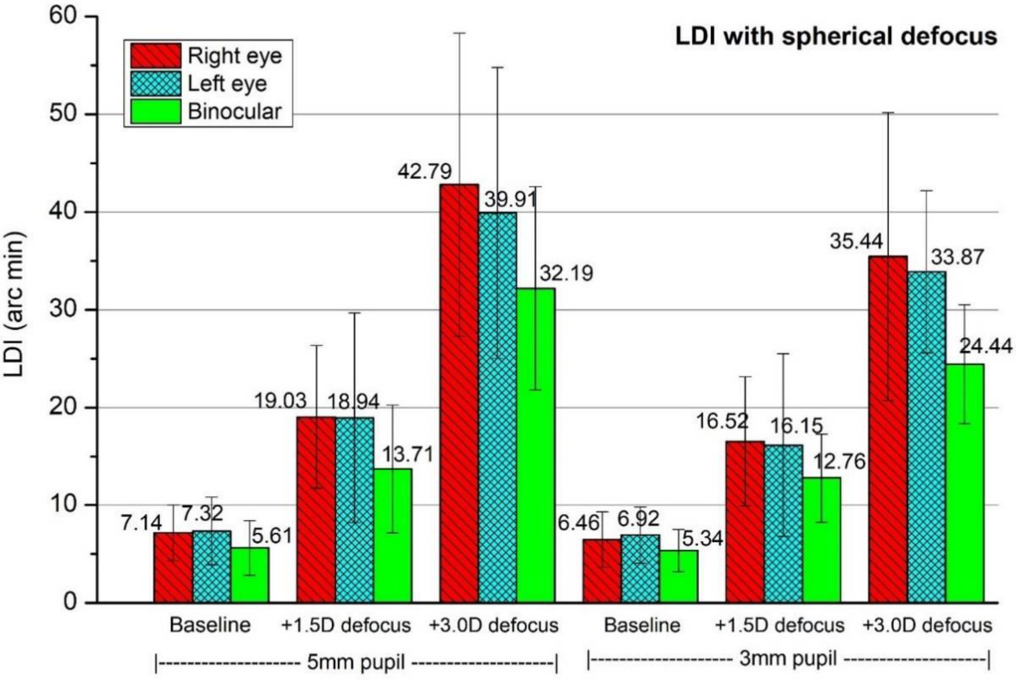
For the HCDVA, the binocular summation increased significantly with pupil size for the +1.5 D spherical defocus ($F_{1,14}$=6.115, p=0.027) and for the +3.0 D cylindrical defocus ($F_{1,14}$=5.210, p=0.039). In the other conditions, binocular summation showed a tendency to improve with larger pupil but with no significant differences ($F_{1,14}$= 2.161, p=0.164 for baseline; $F_{1,14}$= 1.375, p=0.280 for +3.0D spherical defocus; and $F_{1,14}$=0.866, DF=14, p=0.370 for +1.5D cylindrical defocus).

n=15			Binocular summation mean values	
Pupil Size	**Defocus**		**LCDVA**	**HCDVA**
5 mm	Baseline		1.16±0.12	1.10±0.10
	Sph	+1.5 D	1.52±0.24	1.31±0.16
		+3.0 D	1.99±0.59	1.47±0.39
	Cyl	+1.5 D	1.26±0.22	1.23±0.18
		+3.0 D	1.39±0.19	1.44±0.36
3 mm	Baseline		1.07±0.12	1.06±0.06
	Sph	+1.5 D	1.18±0.30	1.16±0.17
		+3.0 D	1.69±0.63	1.39±0.47
	Cyl	+1.5 D	1.12±0.18	1.17±0.20
		+3.0 D	1.22±0.18	1.26±0.24

Table 9. Mean Binocular Summation for the low contrast distance visual acuity (LCDVA) and for the high contrast distance visual acuity (HCDVA) under different levels of cylindrical (Cyl) and spherical (Sph) defocus and different pupil sizes (5 and 3 mm). Standard deviation (SD) included.

5.3.3. Light Disturbance

Figure 18 shows the mean values of the LDI (radius, in minutes of arc) under spherical and cylindrical defocus and the two pupil sizes studied (5 and 3 mm). There were no significant differences between right eye and left eye for all the conditions measured (with a minimum of Z value=-1.59, DF=14, p=0.11 for +3.0 cylindrical). The binocular LDI values asserted a statistically significant difference compared to the same condition monocularly (with of a minimum Z value=2.31, DF=14, p=0.02 for baseline) except for the comparison of the LDI monocular baseline with the binocular LDI baseline under the 3mm pupil condition, with no significant difference (Z value=1.385, DF=14, p=0.17) and neither did the binocular LDI with a spherical defocus of +1.5 D comparing left eye with binocular condition (Z value=1.61, DF=14, p=0.11). As a result, the binocular LDI values were lower than the monocular ones for the pupil sizes analysed, with a significant difference in the most of conditions. Therefore, under monocular conditions, the light disturbance was stronger.



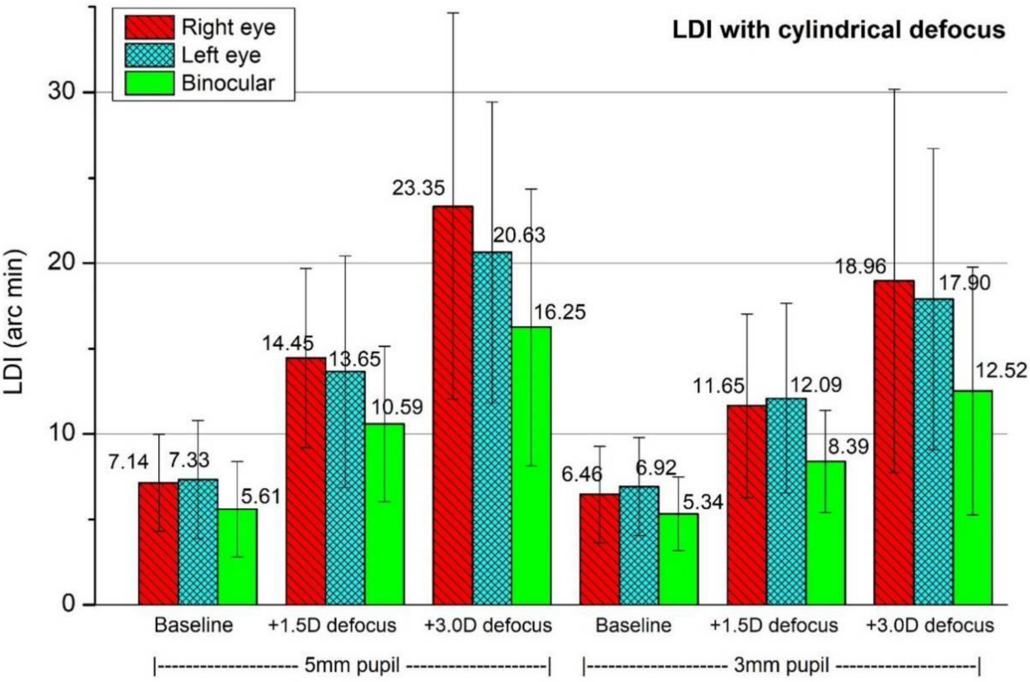


Figure 18. Average and standard deviation values of the light disturbance index (LDI, min arc) under spherical and cylindrical defocus for 3 and 5 millimeters (mm) pupil size condition (n=15). Baseline data (no defocus) are included.

For both pupil size conditions, the monocular and binocular LDI values increased significantly with spherical and cylindrical defocus (Z value=3.11, DF=14, p=0.002). In fact, the LDI proportionally worsened with defocus, showing a stronger effect of the light disturbance on halo perception. With the amount of defocus, the LDI was more deteriorated monocularly than binocularly with statistically significant differences.

Pupil Size	Defocus		LDI Binocular summation mean values (SD), n=15
5mm	Baseline		1.16±0.24
	Sph	+1.5 D	1.22±0.34
		+3.0 D	1.19±0.17
	Cyl	+1.5 D	1.18±0.30
		+3.0 D	1.34±0.54
3mm	Baseline		1.21±0.42
	Sph	+1.5 D	1.16±0.41
		+3.0 D	1.32±0.16
	Cyl	+1.5 D	1.20±0.31
		+3.0 D	1.32±0.19

Table 10. Mean values of the binocular summation for the light disturbance index (LDI) under different levels of cylindrical (Cyl) and spherical (Sph) defocus and different pupil sizes (5 and 3 millimeters, mm). Standard deviation (SD) included.

Table 10 shows a positive binocular summation effect of the LDI for all the experimental conditions. So, the best values were obtained binocularly compared to monocularly (best monocular value of the two eyes). We found no statistically significant differences between 5mm pupil size and 3mm pupil size conditions ($F_{1,14}$=0.184, p=0.675). Only for the +3.0D spherical defocus, the binocular summation disclosed a statistically significant difference ($F_{1,14}$=6.331, p=0.025) between 5mm pupil size and 3mm pupil size. Finally, no statistically significant differences between the different defocus conditions and pupil size conditions (with of a minimum Z value=-1.48, DF=14, p=0.14 between +1.5 cylindrical and +3.0 cylindrical for pupil diameter of 3 mm) were reported.

5.3.4. Correlations

Table 11 shows high statistically significant correlations (p<0.001) between LDI and LCDVA, but also between LDI and HCDVA for all the conditions (defocus and pupil size). Higher coefficient correlations were reported monocularly respect to binocularly in all the conditions. The highest correlations (Spearman R >0.86) were obtained with spherical defocus respect to cylindrical defocus between LDI (a psychophysical parameter) and LCDVA (a visual subjective parameter), but also between LDI and HCDVA (Spearman R >0.85). The pupil size conditions did not show significant differences (p>0.05) comparing their results with the same amount of defocus.

			SPEARMAN R (VA-LDI)		
	Pupil Size	**Defocus**	**Best eye (n=15)**	**Worst eye (n=15)**	**Binocular (n=15)**
LCDVA	5mm	Spherical	0.903	0.908	0.862
		Cylindrical	0.756	0.776	0.688
	3mm	Spherical	0.894	0.931	0.887
		Cylindrical	0.740	0.760	0.645
HCDVA	5mm	Spherical	0.850	0.893	0.866
		Cylindrical	0.738	0.773	0.639
	3mm	Spherical	0.869	0.888	0.863
		Cylindrical	0.715	0.716	0.601

Table 11. Spearman coefficient correlations (Spearman R) between visual acuity (low contrast distance visual acuity, LCDVA; and high contrast distance visual acuity, HCDVA) and the Light disturbance index (LDI) for different levels of defocus and pupil sizes (5 and 3 mm) in monocular and binocular conditions.

5.4. DISCUSSION

The main purpose of the study was to investigate the potential role of the pupil size and defocus on binocular summation for high and low contrast visual acuity and light disturbance metrics. A group of healthy and young subjects was chosen because the factor of age is an important factor which could influence the results of binocular summation (Ross et al., 1985; Pardhan, 1996). The present study shows that binocular summation in healthy and non-surgical patients is consistent under controlled pupil size conditions. In fact, this study has corroborated that might involve essentially a neural factor and not an optical factor because it is not just the result from the expected pupil size reduction under binocular conditions and the quality of the optics forming the retinal image but it could be the ability of the visual cortex to resolve the details of that (Campbell and Green, 1965b; Legge, 1984a; Legge et al., 1987; Plainis et al., 2011).

The control of the pupil size in this study allowed eliminating one important source of interindividual variability. The factor of the pupil size was controlled for two different visual functions: the visual acuity by means of the LCDVA and the HCDVA and the light disturbance by means of the LDI (psychophysical parameters). That’s why the effect of binocular summation was investigated in low and high contrast distance visual acuity and during the light disturbance phenomena under positive spherical and cylindrical defocus.

Firstly, the binocular performance under photopic conditions was analyzed by measuring the low and high contrast visual acuity. The results indicated a strong enhancement of the binocular summation with increased defocus (Atchison et al., 1998). The best binocular visual acuity values were found statistically better in all the levels of defocus for the 3mm pupil size compared to the 5mm pupil size except for the binocular baseline condition. This result could be explained for the high threshold achieved in baseline binocular viewing. Nevertheless, the binocular summation was found to be stronger for the 5mm pupil size in photopic conditions. Moreover, a better binocular summation was achieved in low and high contrast visual acuity with higher spherical defocus compared with baseline and other conditions of cylindrical defocus. As reported by Plainis et al, a higher binocular summation was found in a group of young subjects (i.e. same age mean value) with higher spherical defocus and lower binocular summation for natural condition but not at the same distance for visual acuity (i.e. 1 meter compared with 4 meters in the present research). Also, they have demonstrated that binocular vision improved with the effects of retinal blur on spatial visual performance, but the study was limited since no control of the pupil size was set. These results suggested that the binocular summation for visual acuity task was stronger when the amount of positive defocus increased (Plainis et al., 2011). Similarly, in the present study, stronger binocular advantages were found for a high level of defocus (+3.0D), but also for a lower level of defocus (+1.5D). In the same manner, for higher spherical defocus where the retinal blur is the most relevant, the present results corroborated that the binocular summation increased for low and high contrast visual acuity (Campbell and Green, 1965b; Home, 1978; Legge, 1984a; Gagnon and Kline, 2003) (for +3.0D spherical, LDCVA: 1.99±0.59 and HDCVA: 1.47±0.39). Banton and Levy found that the binocular superiority for low contrast stimuli has also been shown in Vernier acuity (Banton and Levi, 1991). They suggested that in higher contrasts the binocular advantage diminishes due to saturation. Others studies also confirmed higher binocular summation in contrast using masking experiments (studying neural correlates of consciousness and spatiotemporal limits of visual discrimination) (Meese et al., 2006 Baker et al., 2007a). Correspondingly, the increased binocular summation observed with retinal blur may be due to the activation of a larger population of neurons at close-to-threshold detection meaning that less contrast was required under binocular than under monocular stimulation to obtain the same proportion of cells that contribute to contrast detection (Anzai et al., 1995; Plainis et al., 2011) . In another study, Castro et al showed significant differences in contrast sensitivity and visual discrimination between monocular and binocular conditions inducing anisocoria and positive defocus. Due to the interocular differences, they found a deterioration of the binocular summation for the contrast sensitivity function (CSF) after inducing different levels of anisocoria compared with natural conditions. Similar results were found for the visual discrimination index, a parameter which is similar to the LDI, since quantifies the perception of halos (Castro et al., 2016). The present study shows that controlling the pupil size, and avoiding any anisocoria, higher positive defocus is associated to superior binocular summation effects on visual acuity (LCDVA and HCDVA). In other words, binocular summation mechanism provides stronger feedback as the monocular image quality of each eye deteriorates further.

Secondly, the light disturbance phenomenon was measured, by means of the LDI, for different defocus and control pupil size conditions. Under such luminance condition, a better binocular performance was corroborated compared to monocular condition as well as an improvement of the binocular summation when the retinal image was further deteriorated. The binocular summations in the LDI were lower compared with the visual acuity. Recently, Amorim et al found higher light disturbance values in monocular compared to binocular conditions with positive and negative defocus of +1.0D and cyclopegia in young health subject. However, they did not control the pupil size changes between monocular and binocular conditions (Amorim-de-Sousa et al., 2019). Ferreira-Neves et al showed that changing the pupil size from 3 to 6 mm did not have a significant impact on light disturbance in healthy subjects under pharmacologically induced mydriasis with 1% phenylephrine. They showed that the role of the pupil size as a main contributor to light disturbances is not so evident (Ferreira-Neves et al., 2015) . Moreover, Villa et al found a moderate but not significant positive correlation between the pupil size and the magnitude of the light disturbances in eyes undergoing myopic laser-assisted in situ keratomileusis (LASIK) surgery (Villa et al., 2007). The present study did not find statistically significant gain in the binocular summation for the LDI depending on the pupil size except for the highest spherical defocus (better with the pupil size of 3mm). Other works have shown this trend monocularly and binocularly but using a different device (Castro et al., 2016). They found a moderate increase in visual disturbance as pupil size increases, comparing artificial pupils of 2, 3 and 4mm, but with no significant differences. Such differences were justified by a deterioration of the retinal-image quality with pupil size. However, the visual disturbances were significantly greater with natural pupils (mean diameter of 6.5mm) compared to the artificial ones, showing a stronger effect when large differences in pupil sizes were compared.

Comparing with the results obtained by Escandon-Garcia et al in pseudophakic subjects (a mean HCDVA of -0.16±0.27 logMAR; and a mean LDI of 34.6±16.0%, equivalent to a mean halo radius of about 47.6 arc min), the present results show lower values for light disturbance and high contrast distance visual acuity, which is probably due to the fact that the pupil size was controlled (Escandon-Garcia et al., 2018).

Macedo-de-Araujo et al investigated the effect of positive and negative spherical aberration on the light disturbance. They corroborated that light disturbance is sensitive to changes in image quality caused by modifications in spherical aberrations and that accommodation and pupillary constriction are capable of compensating the degradation of the optical quality induced (Macedo-de-Araujo et al., 2016). However, that study did not controlled the pupil size and did not measure under monocular and binocular conditions so the combined effect of induced spherical aberration and pupil size as well as binocular summation was not investigated.

Finally, the present results have shown strong correlations (Spearman R >0.85) between visual acuity and LDI (psychophysical parameters). Hence, the binocularly and monocularly (worst eye) best correlations were obtained with spherical positive defocus (inducing myopia) independently of the pupil size conditions. More specifically, the best correlations were obtained for a 5mm pupil size.

The influence of the accommodation was controlled for young and healthy subjects inducing myopia by defocus. Furthermore, in baseline condition, neither of the subjects recruited had hyperopia. During all our visual measurements, no statistically significant differences were observed between the two eyes of all the subjects and all the conditions measured. In fact, it is known that the interocular differences influence the binocular summation for different visual functions, such as contrast sensitivity or visual discrimination capacity under low-illumination conditions (Sabesan et al., 2012a; Castro et al., 2016).

Limitations of this study include that actual pupil size was not measured during visual acuity and light disturbance evaluation. However, after measuring the pupil with an infrared pupilometer in dim surrounding conditions with the only illumination given mainly by the central LED in the LDA device without trial frame, it is expected that the actual pupil size “behind” the artificial pupil diaphragm would be always larger and not smaller than the reference measurement. The illuminance reaching the eye under light disturbance measurements is lower (0.91±0.02 lx) than for the remaining test conditions to measure visual acuity (170.27±3.86 lx). Even for LDA exam, when the eye is behind the artificial diaphragm to control the aperture during the experiments, the illuminance will be lower and the pupil size expectedly larger. Thought we could not measure the true pupil size during the experiments (behind the artificial diaphragm), it seems reasonable to assume that actual pupil size during experiments is larger than that measured as control with the infrared pupilometer during LDA exposure. Consequently, we should also assume that the artificial pupil at 12 mm is in fact the limiting aperture (3 and 5 mm pupil). During the measurements of the LDI under defocusing conditions, the subjects see a defocused image of the central and peripheral LEDs. This situation corresponds to a similar situation when the subject is in real life trying to discriminate sources of light around a central light source that generates the glare effect.

The present findings could be useful in most of the common emmetropization techniques, such as cataract and refractive surgery or orthokeratology since show the importance of maintaining similar optical characteristics in both eyes and avoiding high interocular differences after surgery in order to preserve a good binocular summation.

In summary, the present results confirm that under the conditions of this study, a positive binocular summation is observed with defocus (spherical and cylindrical) even when pupil size is kept constant. It is observed higher binocular summation with higher defocus and lower contrast induced in visual function. This confirms that under the effect of the defocus in combination with the two control pupil sizes, the binocular summation prevails and increases due to its neural factor (exceeding the optical effect) and not only to an optical one. Further investigation will be required to confirm the part of the neural factor of the binocular summation in the same conditions investigated. It is also confirmed a strong correlation monocularly and binocularly between LDI and visual acuity (especially with spherical defocus induced). This raises an interesting point that suggests light disturbance might be a candidate to psychophysical indicator of the visual potential involving a detection task rather than a recognition task as in the case of visual acuity where other factors such as literacy might influence the measures.

CHAPTER 6

Deterioration of binocular vision after alcohol intake influences driving performance (Study 4)

This study has been published in *Scientific Reports (Martino et al., 2021)*

6.1. INTRODUCTION

Driving under the influence of alcohol represents a serious and significant problem for most countries around the world. According to the World Health Organization (WHO) and its Global Information System on Alcohol and Health (GISAH), more than 3 million people died as a result of harmful alcohol use in 2016 (WHO, 2018), which represents 1 in 20 deaths worldwide. Overall, GISAH statistics establish that the harmful use of alcohol causes more than 5% of global disease burden. Alcohol use is present on road traffic deaths. In 2016, a total of 1,350,000 road traffic deaths were reported, of which 370,000 (27.4%) were related to alcohol consumption (WHO, 2018). Alcohol increases the risk of road accidents and young people represent the population with the greatest risk of being involved in an accident under the effects of alcohol (Deery and Love, 1996; Clarke et al., 2006; Blomberg et al., 2009; Christoforou et al., 2012; Behnood and Mannering, 2017). In the United States of America, over 1,000 college students die each year in an alcohol-related accident (Hingson et al., 2014). Forty-five countries (including the USA and the United Kingdom) still establish their legal limit for breath alcohol content (BrAC) at 0.40 mg/l for driving or the equivalent blood alcohol content (BAC) (WHO, 2018). BrAC and BAC are expressed in milligrams of ethanol per liter of exhaled air (mg/l) and in grams of ethanol per liter of blood, respectively. BAC in g/l is related to BrAC by a ratio of 2:1, in such a way that a BAC of 0.8 g/l (BAC of 0.08%) equals a BrAC of 0.40 mg/l. Driving is a complex task requiring controlled behavior (control over speed, braking, lane position) (Allen et al., 1975; Allen et al., 1996), a high level of concentration and attention, a capacity for quick decisions and reactions, high processing capacities through the central nervous system, and good visual processing (Wood and Owsley, 2005; Owsley and McGwin, 2010; Owsley et al., 2015; Wood and Owsley, 2016). Considering this last point, driving involves the application of different visual functions. In most countries, such as Spain, France, United Kingdom, or the USA, one of the main visual requirements to obtain a driver's license is a visual acuity (on the decimal scale) of greater than or equal to 0.5 (binocularly) or 0.6 (monocularly) (International Council of Ophtalmology, 2006),except in the USA where the minimum monocular visual acuity is 0.5. However, some works have reported that other visual functions have an important impact on simulated driving, e.g., contrast sensitivity, stereoacuity, visual field, eye movements, and retinal straylight (Wood and Owsley, 2005; Owsley and McGwin, 2010; Ortiz et al., 2018a). It is also well known that alcohol consumption deteriorates visual performance, in turn affecting visual acuity, accommodation, contrast sensitivity and glare (Cavalcanti- van Rijn et al., 2011; Galdino et al., 2014; Casares-Lopez et al., 2020b), retinal image quality, and night vision performance (Castro et al., 2014a; Castro et al., 2014b). Furthermore, alcohol inhibits the nervous system, reducing neural processing and transmission (Khan and Timney, 2007) and affecting binocular vision (Brecher et al., 1955). Normal binocular vision is an important factor to take into account in the visual fusion process (Jainta et al., 2015), where the two monocular images are combined into a single one, providing stereoscopic perception and improved visual performance. Visual aspects such as phorias (latent deviation of the visual axes), fusional reserves (positive and negative fusional vergences), and stereopsis are taken into account when assessing the normality of binocular vision. The fusion reflex requires sufficient fusional reserves to achieve phoria compensations. Without fusion reflex, stereopsis (one of the most advanced functions of the visual system), that is, the visual system's capacity to perceive depth, is jeopardized resulting in symptomatic binocular vision. In fact, abnormal binocular vision causes binocular symptoms such as diplopia, blurred vision, headache, and asthenopia (ocular fatigue). Different factors can produce an alteration in normal binocular vision. For example, the use of certain substances, such as cannabis, is known to alter binocular depth inversion (Semple et al., 2003). Sleep deprivation also alters normal convergence, thus increasing the exophoria in near and far vision (Horne, 1975). In this regard, alcohol consumption also diminishes these aspects of binocular vision. Brecher et al found that alcohol produces diplopia and decreases visual convergence (Brecher et al., 1955). Hogan et al determined at distance and near variation in heterophorias causing a deterioration in binocular vision due to the tonic effect on the sixth cranial nerve (Hogan and Linfield, 1983). Munsamy et al found a deterioration in heterophoria, fusional vergences, and the near point of convergence in young healthy subjects at a BrAC of 0.1% (0.50 mg/l) (Munsamy et al., 2016). Our hypothesis is that deterioration in the binocular visual system due to a moderate alcohol intake could influence driving performance, since driving is a complex task involving several visual functions. In this manner, driving performance could correlate with the deterioration of visual performance showing a causal relationship. No previous studies have characterized the deterioration of the overall binocular visual performance and driving ability after alcohol consumption, particularly when considering the legal limit of 0.40 mg/l of alcohol established for driving in most countries.

With this in mind, the aim of the study was to assess the influence of a moderate alcohol content (BrAC) of 0.40 mg/l on binocular visual performance (by means of visual acuity, stereopsis and fusional vergences) in healthy young subjects with normal binocular vision, and investigate how this affects simulated driving performance. It is the first experimental study to analyze the effects of binocular visual performance on driving performance under the influence of a moderate alcohol intake through several binocular visual parameters, including visual acuity, stereopsis, phorias, fusional reserves, AC/A ratio (the amount of convergence affected by the change in the accommodation), Sheard's and Percival's criteria (criteria assessing the correct compensation of the phoria and, in consequence, binocular vision comfort), and vergence facility (capacity of the visual system to respond accurately to vergence changes in a limited time).

6.2. METHODS

6.2.1. Subjects and Procedure

The study was approved by the Human Research Ethics Committee of the University of Granada (921/CEIH/2019). Prior to participating in the study, all participants signed an informed consent form in accordance with the Helsinki Declaration, including information on the purpose of the study, the methods used, and the amount of alcoholic beverage they would have to drink. A total of 30 healthy subjects (13 females, 17 males) ranging from 21 to 40 years (26.3 ± 4.4) were recruited in this crossover study. They had a mean body mass index (BMI) of 22.5 ± 2.9 kg/m². The inclusion criteria were: best-corrected monocular visual acuity ≥ 1.0 (decimal notation), no ocular diseases or binocular disorders (normal phorias and stereopsis), being a social drinker with a score of 8 or less on the alcohol use disorders identification test (AUDIT) (Saunders et al., 1993; Charlton and Starkey, 2015; Verhoog et al., 2020), and not presenting driving simulator sickness (Matas et al., 2015). In addition, our study cohort comprised a healthy young population with normal binocular vision, as this is the most typical driving situation for most drivers. We choose a group of healthy young subjects because age is an important factor that could influence the results for the binocularity (Pardhan, 1996), driving (Fildes et al., 2007; Matas et al., 2015; Guinosso et al., 2016), and driving simulator sickness (Matas et al., 2015). None of the participants were under pharmacological treatment or had pathological conditions that could be affected by alcohol intake. All participants had had a driving license for at least two years, and they drove at least 2,000 km/year. The participants' mean refractive error (spherical equivalent) was -1.11 ± 1.69 D. The mean pupil size in baseline conditions was of 5.6 ± 0.5 mm. We measured the pupil diameter with the Colvard pupilometer (OASIS Medical, Inc. Glendora, California, USA).

Participants took part in two sessions: the first session under natural conditions (baseline) and the second after alcohol consumption (aAC). The two sessions were performed on different days, with an interval of one week between them, to avoid any ocular fatigue and diminish order effects, just as shown by other studies (Ortiz et al., 2018a; Casares-Lopez et al., 2020a). In the alcohol-intake session, the breath alcohol content (BrAC), defined in milligrams of ethanol per liter of exhaled air (mg/l), was measured using the Dräger Alcotest 6810 (Dräger Safety AG& Co. Lubeck, Germany) breath analyzer which provides good reproducibility(Hackett et al., 2017). Participants consumed a mixed alcohol beverage (67% orange juice and 33% vodka). They had to reach a BrAC of 0.40 mg/l, and the mean BrAC measured for all participants was 0.40 ± 0.03 mg/l. We used an improved version of the Widmark formula (Watson et al., 1981) to calculate the alcohol intake required for each participant to reach this BrAC. Each participant consumed the corresponding alcohol dose within a 30–40 minute period. During the second session, we measured the BrAC every 20 minutes after consuming the alcoholic beverage, so we measured the BrAC five times in total, monitoring for a BrAC of about 0.40 mg/l. All the visual tests were randomized in the two experimental sessions (baseline and aAC) to avoid learning effects influencing the results. The subjects were aware they were consuming alcohol in order to test them in a common real-world situation.

6.2.2. Visual performance

Visual acuity and stereopsis

A full eye examination, including objective and subjective refraction using the endpoint criterion of maximum plus for best visual acuity, was conducted monocularly and binocularly at distance (5.5 m) under photopic conditions. In this manner, the best visual acuity at distance (decimal notation) was measured binocularly under photopic lighting conditions. Stereoacuity was also measured using two different tests: the VistaVision monitor stereotest (DMD MedTech, Villarbasse, Torino, Italy) at distance (5.5 m), and the Randot stereotest (Stereo Optical, Inc., Chicago, USA) at near (40 cm), the latter commonly used in clinical practice. Distance stereoacuity was measured using polarized vertical lines displayed on the monitor. For this, a total of 8 disparities from 300 to 10 arc sec were evaluated. For each disparity, five vertical lines were displayed simultaneously along a row on the monitor, one of which showed a disparity to be perceived stereoscopically. For both tests (distance and near), the observer wore polarized glasses and the task was to recognize stimuli perceived stereoscopically.

Phorias and fusional vergences

Phoria is defined as the locus (center) of intersection of the lines of sight, measured with respect to the object of regard, in the absence of a fusional vergence response (Rosenfield et al., 2000). Under photopic conditions, distance and near-dissociated phorias (horizontal and vertical) were measured with a phoropter using Von Graefe's method (Antona et al., 2008). In addition, positive and negative fusional vergences (blur, break, and recovery points) were also determined at distance (5.5 m) and near (40 cm) using the phoropter's Risley rotary prism, which provides high reproducibility and accuracy (Rosenfield et al., 1995; Antona et al., 2008; Goss and Becker, 2011). These parameters were reported in prism diopters (Δ).

We also used two methods to calculate the AC/A (accommodative convergence/accommodation) ratio: calculated (Eq. 3) and gradient (Eq. 4).

The AC/A ratio is determined by the amount of accommodative convergence induced by a change in accommodation. AC/A values are reported in prism diopters per accommodation diopter (Δ/D). It is an important and stable factor (Rosenfield et al., 2000) when trying to understand the relation between these two values (Wybar, 1974). In addition, Percival's and Sheard's criteria were evaluated to ascertain the presence of any binocular vision alterations. Percival's criterion defines a rule to anticipate visual discomfort in connection with fusion ranges: the point-of-zero demand should fall in the middle third of the total fusional vergence for comfortable binocular vision (Sheedy and Saladin, 1978). According to Sheard's criterion, the amount of heterophoria should be less than half the opposing fusional convergence in reserve. Sheard's criterion is a good discriminator for exo deviations, and Percival's criterion is good for eso deviations (Sheedy and Saladin, 1978). In our study, a negative value for these criteria (measured in prism diopters, Δ) corresponds to the correct compensation of the respective phoria being measured. In contrast, a positive value represents a decompensated phoria.

We also evaluated vergence facility (VF), which assesses the ability of the fusional vergence system to respond to changes in vergence demands over time. VF is defined as the number of cycles per minute (cpm) through which a stimulus can be fused based on alternating base-in (BI) and base-out (BO) prisms (Gall et al., 1998). Optimal reproducibility and accuracy was attained with a near VF test (at 40 cm) was used with a flipper prism of 3Δ BI and 12Δ BO (Gall et al., 1998). VF was used to detect any binocular vision problems (Gall and Wick, 2003). We repeated the measurement of all vergence parameters three times for each participant in both baseline conditions and after alcohol consumption. The normal range of vergence facility is considered to be between 10 and 15 cpm (Gall and Wick, 2003; Momeni-Moghaddam et al., 2014).

Visual performance deterioration

Finally, an overall visual deterioration score (OVDS) was obtained by averaging the z-scores of the deterioration (difference between the aAC and baseline values) of the visual variables including visual acuity, stereoacuity, horizontal and vertical phorias, horizontal negative and positive fusional vergences, vertical fusional vergences, and vergence facility. Equal weight was assigned to all the visual variables. We multiplied the z-scores of some variables by -1, so that for all the variables the more positive the score, the greater the visual deterioration and the worse the visual performance. Z-scores have been widely used (Wood, 2002; Casares-Lopez et al., 2020a; Ortiz-Peregrina et al., 2020a; Ortiz-Peregrina et al., 2020c) and are a measurement of how many standard deviations an individual value is away from the group mean.

6.2.3. Simulated driving and driving performance

A driving simulator represents an accurate means of analyzing driving-related parameters (Tornros, 1998; Shechtman et al., 2009). Simulated driving was carried out under photopic lighting conditions, which represent the best conditions for driving performance (Alferdinck, 2006; Pritchard and Hammett, 2012). The driving simulator used in this study consists of three high definition 27” screens (resolution of 1,920×1,080 pixels) with 180 degrees field of view, a car seat, and the Logitech G27 Racing Wheel (Logitech International SA, Lausanne, Switzerland) comprising a steering wheel, gearshift (six speeds and reverse), and three pedals (accelerator, brake, and clutch). Simax Driving Simulator v4.0.8 Beta software (SimaxVirt S.L., Pamplona, Spain) was used for the driving simulations (Ortiz et al., 2018a). The driving scenario, with an itinerary of approximately 12.5 km, was performed in daylight and under good weather conditions. It consisted of three main sections simulating different road environments with moderate traffic. The first section was a 4.5 km long dual carriageway with a speed limit of 120 km/h. The second section was a 6 km single carriageway mountain road with a speed limit ranging from 40 km/h to 90 km/h. The third section was a 2 km inner-city circuit with a speed limit of 40-50 km/h. Participants came to the laboratory at least four times in four separate weeks. All participants received at least two training sessions (separated by a one week interval) to help them acclimatize to the driving simulator (Hall and West, 1996) but also to minimize learning effects as shown in other works (Casares-Lopez et al., 2020a; Ortiz et al., 2018a). During the first training session (week 1), participants completed one full lap of the simulated driving scenario (12.5 km). In the second training session (week 2), participants completed another one full lap of the driving scenario (12.5 km) and performed all visual tests once (results from these tests were not used in the analysis). In both the baseline session (week 3) and the aAC session (week 4) participants carried out one full lap of the driving scenario and performed all visual tests. In these sessions, the visual tests and simulated driving scenario were randomly performed across participants (visual tests were performed before or after the simulated driving). Only results from the baseline and aAC sessions were analyzed. All subjects were instructed to drive normally, while respecting traffic laws. The following variables were measured in order to assess driving performance: mean speed and standard deviation (km/h), distance traveled invading the shoulder (DTIS, m), distance traveled invading the opposite lane (DTIOL, m), total distance traveled outside the lane (TDTOL, m), standard deviation of the lateral position (SDLP, m), and reaction time (s). The reaction time was calculated as the interval between the instant the brake lights turned on in the preceding car and the moment the driver pressed the brake pedal. We also recorded the number of collisions, signaling mistakes, and engine stalls. The SDLP is known to be a valid indicator of impaired behavior with and without alcohol (Helland et al., 2013; Freydier et al., 2014; Ortiz et al., 2018a; Ortiz-Peregrina et al., 2020c). In line with the OVDS calculation, but also with other studies (Wood, 2002; Casares-Lopez et al., 2020a; Ortiz-Peregrina et al., 2020c;), an overall driving performance deterioration score (ODPDS) was also calculated, averaging the z-scores of the deterioration of driving variables included in the three sections: mean speed and standard deviation, DTIS, DTIOL, TDTOL, SDLP, reaction time, collisions, signaling mistakes and engine stalls. In this study, the higher the ODPDS values, the greater the driving performance

6.2.4. Statistical procedures

The statistical analysis was performed using SPSS Statistics v.23.0 software (SPSS Inc., Chicago, IL). The normality of the sample was checked using the Kolmogorov–Smirnov test (n=30). If the data were normally distributed, a t-test for two-sided alternatives was performed to compare each visual and driving variable separately for the two experimental conditions (baseline and aAC). Similarly, the Wilcoxon signed rank test was used in the case of no normal distribution. The Holm-Bonferroni method to control the family-wise error rate was applied. We also noted the degrees of freedom (DF). Finally, a Spearman correlation analysis was used to study the relationship between the visual deterioration (OVDS) and the driving performance deterioration (ODPDS) scores providing the correlation factor rho (ρ) and the corresponding p-values. Differences were considered statistically significant for p-values < 0.05.

6.3. RESULTS

6.3.1. Visual performance

Visual acuity and stereopsis

Table 12 shows the mean values for pupil diameter and binocular vision function parameters measured under natural conditions (baseline) and after alcohol consumption (aAC). Statistically significant deteriorations were found after alcohol consumption for distance visual acuity (Z= -4.73, DF= 29, p<0.001), and distance (Z = -4.61, DF = 29, p<0.001) and near (Z = -4.45, DF = 29, p<0.001) stereoacuity. A significant increase in pupil diameter was also observed (Z = -5.58, DF = 29, p<0.001). As a result, there was a decline in binocular vision parameters for visual acuity and stereoacuity after an alcohol intake that achieved a BrAC level of 0.40 mg/l.

		Baseline	aAC	p-value	impairment (aAC-Baseline)
Pupil diameter (mm)		5.6 ± 0.5	6.3 ± 0.6	< 0.001	0.7 ± 0.5
Distance VA (decimal)		1.35 ± 0.15	1.09 ± 0.15	< 0.001	-0.26 ± 0.14
Stereoacuity (arc sec)	Distance	25 ± 16	118 ± 91	< 0.001	94 ± 86
	Near (Randot)	20 ± 6	36 ± 13	< 0.001	16 ± 11

Table 12. Mean and standard deviations of pupil diameter and binocular vision function parameters (distance visual acuity and stereopsis) measured at baseline and after alcohol consumption (aAC) giving a BrAC of 0.40 mg/l. Mean impairment values for each parameter are included (calculated as the mean difference between aAC and baseline conditions).

Phorias and fusional vergences

Figure 19 shows the mean values of the distance negative fusional vergences (NFV) and positive fusional vergences (PFV) in the baseline condition and after alcohol consumption (BrAC = 0.40 mg/l), while Figure 2 depicts distance phorias (horizontal and vertical) at baseline and after alcohol consumption (BrAC = 0.40 mg/l).

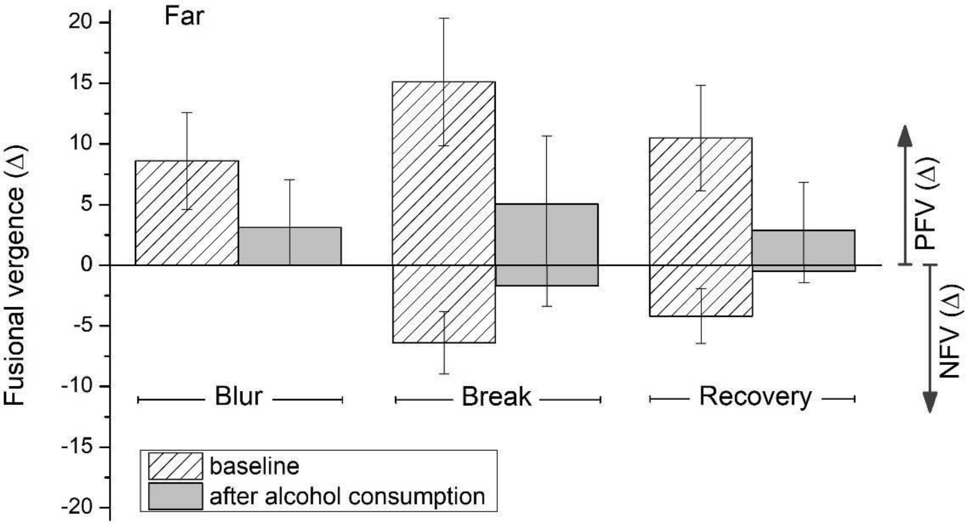


Figure 19. Mean values for the horizontal fusional vergences at distance at baseline and after alcohol consumption (BrAC = 0.40 mg/l). Blur, break, and recovery are shown for the negative (NFV) and positive (PFV) fusional vergences. Error bars show standard deviations.

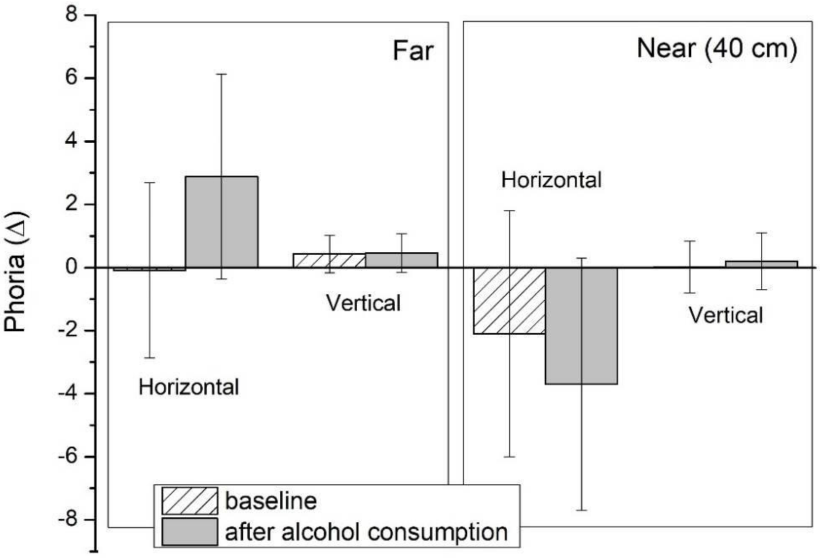


Figure 20. Mean values for distance and near phorias (horizontal and vertical) at baseline and after alcohol consumption (BrAC = 0.40 mg/l). Error bars show standard deviations.

According to Table 13 and Figures 19 and 20 all the distance negative and positive fusional vergences (horizontal and vertical) decreased significantly after consuming alcohol (BrAC = 0.40 mg/l) compared to the baseline session ($p<0.001$). All the distance vergence parameters measured at baseline were within normal standard values (Morgan, 1944; Sheedy and Saladin, 1977). Moreover, a statistically significant difference was observed and the distance horizontal phoria changed its direction significantly, becoming more esophoric after alcohol consumption ($Z = -4.37$, $DF = 29$, $p<0.001$), with a mean value of 2.9 ± 3.2 Δ. In contrast, we did not observe a statistically significant deterioration in the vertical phoria following alcohol consumption ($Z = -0.47$, $DF = 29$, $p=0.638$). In addition, Sheard's and Percival's criteria were also checked. These criteria assess the correct compensation of the respective phoria measured and the binocular visual discomfort. In Table 13, a negative value for these criteria corresponds to the correct compensation of the respective phoria and, in contrast, a positive value represents a decompensated phoria and binocular visual discomfort. Both criteria employed at distance showed statistically significant deteriorations under the effects of alcohol: Sheard's criterion, ($Z = -4.66$, $DF = 29$, $p<0.001$) and Percival's criterion, ($Z = -3.52$, $DF = 29$, $p<0.001$). Consequently, Sheard's criterion at distance had a positive mean value after alcohol consumption revealing a decompensated phoria and, therefore, binocular visual discomfort in our subjects.

Figure 20 represents the mean values of the near phorias (horizontal and vertical), while Figure 21 shows the near negative (NFV) and positive fusional vergences (PFV) under natural conditions and after alcohol consumption.

Far		**Baseline**	**aAC**	**p-value**	**Impairment (aAC-baseline)**
Vertical FV (Δ)	Break	2.2 ± 0.6	0.9 ± 1.0	<0.001	-1.2 ± 1.1
	Recovery	0.9 ± 0.5	0.1 ± 0.3	<0.001	-0.8 ± 0.5
Percival's criterion (Δ)		-1.4 ± 2.3	-0.1 ± 1.4	<0.001	1.3 ± 1.8
Sheard's criterion (Δ)		-2.4 ± 2.3	1.3 ± 2.5	<0.001	3.7 ± 2.4

Table 13. Mean values and standard deviations for distance vertical fusional vergences and Percival's and Sheard's criteria, measured at baseline and after alcohol consumption (aAC) for a BrAC of 0.40 mg/l. Mean impairment value for each parameter and p-values of the mean comparisons are included.

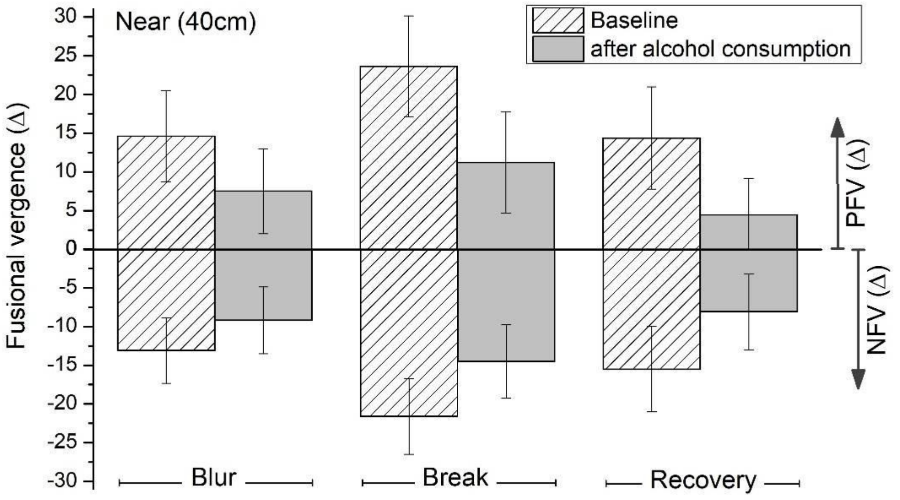


Figure 21. Mean values for the horizontal fusional vergences at near distance at baseline and after alcohol consumption (BrAC = 0.40 mg/l). Blur, break, and recovery are shown for the negative fusional vergences (NFV) and positive fusional vergences (PFV). Error bars show standard deviations.

Similarly, Table 14 and Figures 20 and 21 show all the parameters of the near phorias and fusional vergences, as well as their criteria and AC/A ratios. All the near vergence parameters measured under natural conditions (baseline) were within normal standard values (Morgan, 1944; Sheedy and Saladin, 1977). All the near negative and positive fusional vergence (horizontal and vertical) values decreased significantly after consuming alcohol (BrAC = 0.40 mg/l) compared with baseline (Z = -4.13, DF = 29, p<0.001). A decrease of the near horizontal phoria was observed between the baseline condition and after alcohol consumption, but not statistically significant (p=0.078). Likewise, no statistically significant deterioration was found for near vertical phoria (Z = -0.69, DF = 29, p=0.488). At near, no significant changes were reported for the Sheard and Percival's criteria. Statistically significant deterioration was evident for the vergence facility after consuming alcohol (t(29) = 11.062, p<0.001) and also for both AC/A ratios: for calculated AC/A ratio (t = 4.47, DF = 29, p<0.001) and for gradient AC/A ratio (Z = -3.71, DF = 29, p<0.001). As a result, the binocular vision was also significantly affected at near.

Near		Baseline	aAC	p-value	Impairment (aAC-Baseline)
Vertical FV (Δ)	Break	3.6 ± 1.3	2.3 ± 1.0	<0.001	-1.3 ± 1.1
	Recovery	2.0 ± 1.0	0.4 ± 0.5	<0.001	-1.6 ± 0.8
Vergence Facility (cpm)		14.1 ± 2.8	8.6 ± 3.4	<0.001	-5.5 ± 2.7
Percival's criterion (Δ)		-3.8 ± 2.6	-3.6 ± 2.9	0.655	0.2 ± 2.3
Sheard's criterion (Δ)		-6.2 ± 3.5	-4.7 ± 2.9	0.078	1.5 ± 3.7
Calculated AC/A ratio (Δ/D)		5.3 ± 1.4	3.6 ± 1.5	<0.001	-1.7 ± 2.1
Gradient AC/A ratio (Δ/D)		4.1 ± 1.9	2.3 ± 1.0	0.007	-1.8 ± 2.2

Table 14. Mean values and standard deviations for near vertical fusional vergences, vergence facility, Percival's and Sheard's criteria, and AC/A ratio measured at baseline and after alcohol consumption (aAC, BrAC = 0.40 mg/l). Mean impairment values for each parameter and p-values of the mean comparisons are included.

6.3.2. Simulated driving performance

Table 15 shows all the parameters measured at baseline and after alcohol consumption (aAC, BrAC = 0.40 mg/l) that characterize driving performance. All the parameters analyzed in the three sections (dual carriageway, two-lane mountain road and inner city) deteriorated significantly ($p<0.05$) except signaling mistakes ($p=0.078$). Mean speed in the three sections was higher with BrAC = 0.40 mg/l compared to the alcohol-free baseline session. After consuming alcohol, the mean speed in the dual carriageway section was 129.4 ± 13.9 km/h, above the legal speed limit of 120 km/h. Furthermore, the mean speed significantly increased with alcohol intake compared to baseline ($t(29) = 4.90$, $p<0.001$). Participants drove significantly more distance invading the opposite lane and also veered more distance invading on the shoulder after consuming alcohol ($Z = -3.94$, $DF = 29$, $p<0.001$). The SDLP (standard deviation of the lateral position) of simulated driving was significantly higher after alcohol consumption in the dual carriageway ($Z = -4.41$, $DF = 29$, $p<0.001$) and in the two-lane mountain road, ($t(29) = 8.28$, $p<0.001$). Furthermore, a statistically significant increase was also found for the mean reaction times with alcohol consumption ($t(29) = 4.83$, $p<0.001$). The number of collisions was higher with alcohol consumption showing a statistically significant deterioration ($Z = -4.55$, $DF = 29$, $p<0.001$). As a result, simulated driving following alcohol consumption (BrAC = 0.40 mg/l) represented a risk for road safety.

		Baseline	aAC	p-value	Change/impairment (aAC-Baseline)
Dual carriageway	MS (km/h)	116.9 ±4.9	129.4 ± 13.9	<0.001	12.5 ± 14.0
	MSSD (km/h)	8.0 ± 3.0	11.5 ± 4.9	0.012	3.5 ± 5.7
	SDLP (m)	0.54 ± 0.12	0.75 ± 0.22	<0.001	0.21 ± 0.18
	DTIS (m)	90.0 ± 119.2	267.8 ± 231.3	<0.001	177.8 ± 196.4
Two-lane mountain road	MS (km/h)	55.5 ± 1.4	58.4 ± 5.4	0.035	2.8 ± 5.1
	MSSD (km/h)	21.4 ± 2.2	23.9 ± 5.0	0.048	2.5 ± 5.2
	SDLP (m)	0.55 ± 0.09	0.76 ± 0.16	<0.001	0.21 ± 0.14
	DTIS (m)	43.0 ± 58.6	227.8 ± 257.3	<0.001	184.8 ± 238.4
	DTIOL (m)	309.4 ± 241.5	562.1 ± 418.2	<0.001	252.7 ± 334.4
	TDTOL (m)	352.5 ± 227.9	789.9 ± 478.8	<0.001	437.5 ± 404.5
	RT (s)	0.82 ± 0.13	0.93 ± 0.14	<0.001	0.11 ± 0.12
Inner city	MS (km/h)	30.5 ± 4.6	36.1 ± 6.4	0.008	5.5 ± 8.1
	MSSD (km/h)	16.4 ± 3.4	21.2 ± 5.7	<0.001	4.7 ± 5.8
Events	Collisions (times)	0.1 ± 0.3	4.3 ± 3.7	<0.001	4.3 ± 3.6
	SM (times)	0.0 ± 0.0	0.3 ± 0.8	0.078	0.3 ± 0.8
	ES (times)	1.3 ± 1.3	3.8 ± 4.4	0.009	2.5 ± 4.3

Table 15. Mean values and standard deviations for all the simulated driving parameters, measured at baseline and after alcohol consumption (aAC; BrAC = 0.40 mg/l), including the mean change for each parameter, calculated as the averaged difference between aAC and baseline values. (MS: mean speed; MSSD: mean speed standard deviation; SDLP: standard deviation of the lateral position; DTIS: distance traveled invading the shoulder; DTIOL: distance traveled invading the opposite lane; TDTOL: total distance traveled outside the lane; RT: reaction time; SM: signaling mistakes; ES: engine stalls).

6.3.3. Correlation between visual and driving performance

Figure 22 shows the relationship calculated between the overall visual deterioration (OVDS) and the overall driving performance deterioration (ODPDS). A positive statistically significant correlation ($\rho = 0.390$, $p=0.033$) was found between OVDS and ODPDS, revealing that the greater the deterioration in this overall visual function, the greater the impairment in the driving performance measured. For this reason, degradation in the vergence system and stereoacuity at near and distance, as well as visual acuity, correlate with a consequent deterioration in driving performance. The correlation between OVDS and

ODPDS would be greater and more significant if we deleted the outlier (OVDS = -0.83, ODPDS = 1.50) from the statistical analysis (ρ = 0.528, p=0.003).

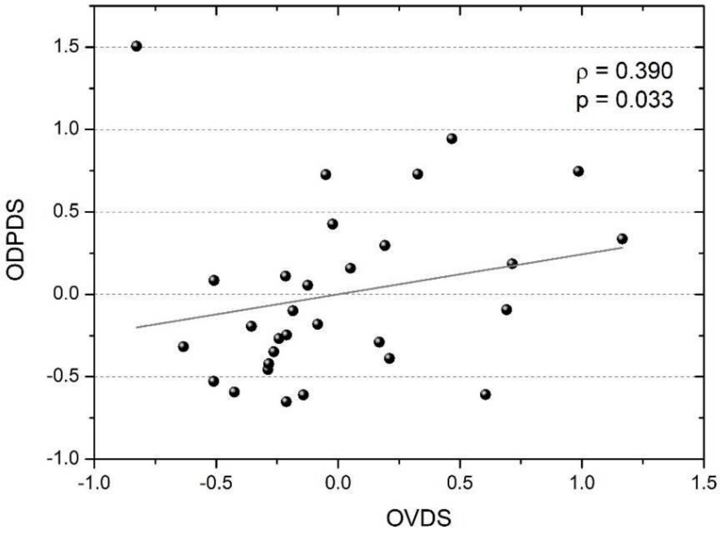


Figure 22. The overall visual deterioration score (OVDS) as a function of the overall driving performance deterioration score (ODPDS).

6.4. DISCUSSION

This study provides an overview of the influence of alcohol consumption (BrAC of 0.40 mg/l) on binocular visual performance and simulated driving in healthy young subjects with normal binocular vision, corresponding to the most typical visual condition. We assessed binocular visual performance by means of parameters such as visual acuity, stereoacuity, and near and distance vergence function (phorias, NFV, PFV, AC/A ratio, vergence facility, Sheard's and Percival's criteria). Simulated driving performance was characterized by driving parameters for the three road environments: mean speed, SDLP, distance traveled invading the opposite lane, distance traveled invading on the shoulder, total distance traveled outside the lane in the two-lane mountain road, reaction time, signaling mistakes, engine stalls, and number of collisions. All the binocular visual and vergence functions and simulated driving parameters showed a statistically significant impairment following alcohol intake, except near horizontal phoria, near and distance vertical phoria, near Sheard's and Percival's criteria and signaling mistakes. In fact, for some parameters measured, distance vergence function showed a greater deterioration after alcohol consumption than near vergence function, except for positive and negative fusional vergences. To the best of our knowledge, there are no previous findings showing correlations between binocular visual performance impairment, specifically vergence function parameters, and deterioration in simulated driving performance due to alcohol consumption. In addition, studying the influence of alcohol consumption on binocular vision and driving performance at the legal BrAC limit of 40 mg/l (BAC of 0.8 g/l or 0.08%) is of special interest for road traffic applications. For the driving task, the present study shows impairment for a BrAC of 0.40 mg/l. Even though the most common legal limit of BrAC worldwide is 0.25 mg/l (BAC of 0.5 g/l or 0.05%), for example in Spain and 51 other countries(WHO, 2018), we chose a BrAC of 0.40 mg/l because it is still the legal limit for driving in 45 countries around the world, including the UK and the USA(Kahn, 2015; WHO, 2018). Therefore, another aim of this study was to quantify and simulate binocular visual impairment during a highly demanding visual task such as driving. The study evidenced a high deterioration in simulated driving and binocular visual at a BrAC of 0.40 mg/l, as it caused adverse effects in the visual system and diminished driving safety.

Firstly, we analyzed binocular vision function by measuring visual acuity under photopic conditions. Alcohol consumption caused a statistically significant deterioration of 0.26 (decimal notation). As reported by Lee et al alcohol consumption is associated with a deterioration of visual acuity (Lee et al., 2010),. Some investigations have shown that alcohol consumption also negatively affects other visual functions. Castro et al found a deterioration in visual discrimination capacity in night-vision conditions after drinking red wine. They also found an increase, on average, in pupil diameter in dim surrounding conditions after consuming red wine (mean BrAC of 0.32 ± 0.14 mg/l; mean increase in pupil diameter of 0.4 mm) and a deterioration of retinal image quality (Castro et al., 2014a; Castro et al., 2014b). Other authors have also reported an increase in intraocular straylight after consuming alcohol and a deterioration in binocular contrast sensitivity function (Casares-Lopez et al., 2020a). The present study corroborates an increase of mean pupil diameter (0.7 mm) induced by a BrAC of 0.40 mg/l which could contribute to poorer retinal image quality (Castro et al., 2014b). In addition, we found that near and distance stereoacuity also deteriorated following alcohol consumption. The impairment was higher in distance stereoacuity (94 arc sec) compared to near stereoacuity (16 arc sec). Wegner and Fahle(Wegner and Fahle, 1999) observed a significant deterioration (93 arc sec) in distance stereoacuity after consuming alcohol (a BAC from 0.8 to 1.3 g/l). Watten and Lie also found near stereoacuity deterioration (32 arc sec) with higher alcohol consumption (BrAC of 0.50 mg/l) than in our study (Watten and Lie, 1996). Stereopsis represents the highest level of binocular vision and is necessary for effective efficient binocular vision quality. A greater impairment in distance stereoacuity implies a deterioration in depth perception and therefore the visual system has a lesser capacity to estimate relative distances. Alcohol consumption had a negative effect on stereoacuity and, consequently, binocular vision performance.

Secondly, to maintain normal and efficient binocular vision and avoid diplopia, sufficient fusional reserves are required to compensate horizontal phoria. Otherwise, subjects may experience visual discomfort, causing tropia, amblyopia, and strabismus. In the present study, results showed that fusional reserves decreased significantly with alcohol consumption, compromising normal binocular vision. In fact, the mean horizontal phoria at distance in the baseline session was -0.1 Δ exophoria (normal healthy population) and after consumption was 2.9 Δ esophoria, which represents an average that falls outside normal values for a healthy population (Morgan, 1944; Sheedy and Saladin, 1977). So, a mean increase of 3 Δ in esophoria was observed with a BrAC of 0.40 mg/l. This is in line with others studies which reported a change towards a more esophoric distance horizontal phoria with alcohol consumption (McNamee et al., 1981; Hogan and Linfield, 1983; Munsamy et al., 2016). Hogan and Lindfield suggested that ethanol has a toxic effect on the sixth cranial nerve, causing an increase in distance esophoria and subsequently convergent strabismus (Hogan and Linfield, 1983). Owens and Leibowitz assumed that alcohol induces esophoria for distance vision, thus causing a regression of vergence toward a tonic position (Owens and Leibowitz, 1983). A possible explication could be that alcohol consumption changes the visual axes towards a convergent position and produces a possible decline in the lateral recti's ability to contract/relax at distance, thereby impacting on neuromuscular control. On the other hand, for near horizontal phoria, we observed a mean increment (but not significant) of exophoria (1.6 Δ) for a BrAC of 0.40 mg/l. This result is in line with Hogan and Linfield who found an increase in exophoria for near horizontal phoria of 2 Δ (Hogan and Linfield, 1983). Munsamy et al also observed a significant increase in exophoria of 1 Δ for a BrAC of 0.50 mg/l (Munsamy et al., 2016). So, for near horizontal phoria, alcohol has a negative effect, deflecting the visual axes towards a divergent position, possibly due to an inhibition of the medial recti muscle. Wilson and Mitchell associated the increase of exophoria at near with a reduction in muscle tonus and reported that it increased with the amount of alcohol consumed (Wilson and Mitchell, 1983).

We did not find any significant differences for vertical phoria at near and distance, suggesting that alcohol consumption at a BrAC of 0.40 mg/l does not affect vertical muscles and visual axes (Hogan and Linfield, 1983; Wilson and Mitchell, 1983; Munsamy et al., 2016). Munsamy et al found significant impairments in horizontal positive and negative fusional vergences after alcohol consumption (BrAC of 0.25 mg/l and 0.50

mg/l) (Munsamy et al., 2016). In our study, we confirmed that all the mean horizontal positive and negative fusional vergences decreased significantly at near and at distance after consuming alcohol (BrAC of 0.40 mg/l). Moreover, in the break and recovery points, a BrAC of 0.40 mg/l induced a statistically significant impairment of fusional reserves, causing a significant impairment in the Percival's and Sheard's criteria at distance. Furthermore, the mean Sheard's criterion at distance was positive (1.3 Δ), which would cause significant discomfort in binocular viewing conditions (this value is indicative of the need for a prism prescription due to weak binocular vision). Hence, Sheard's criterion might be of interest when assessing binocular vision in driver eyesight. Hence, the legal alcohol content of 0.40 mg/l, still in force in many countries, weakened binocular fusional reserves, leading to the risk of misaligned visual axes and decompensated phoria. This could induce a collapse in distance phoria from a latent to a manifest deviation resulting in a deterioration of normal binocular vision (strabismus and/or diplopia) (Brecher et al., 1955; Hogan and Linfield, 1983). Miller et al stipulated that the general effect of alcohol is to produce a decrease in vergence range manifesting as changes in both fusional and accommodative vergence (Miller et al., 1986). In fact, in our study, the mean significant decrease and deterioration were apparent in the calculated AC/A ratio (1.7 Δ) and in the gradient AC/A ratio (1.8 Δ). Cohen and Alpern also found a decrease in the AC/A ratio for moderate alcohol intake (Cohen and Alpern, 1969), whereas Hogan and Linfield did not find a significant change in the AC/A ratio for a low alcohol intake (Hogan and Linfield, 1983). Rosenfield et al suggested that the oculomotor crosslinks are innervated by the combined output of the fast and slow controllers and the accommodative convergence by fast and slow blur-driven accommodation, which implies that alcohol consumption could have a toxic effect (Rosenfield et al., 2000). The mean vergence facility at near was impaired at a BrAC of 0.40 mg/l. In fact, for this parameter, alcohol consumption induced a statistically significant deterioration of 5.5 cpm, which agrees with our results which indicate weakness of binocular visual performance.

A change from natural to less natural conditions due to alcohol consumption led to a decrease in vergence facility (Momeni-Moghaddam et al., 2014). Vergence facility represents a clinically useful parameter for the diagnosis of binocular vision abnormalities, and is closer to the dynamic character of real-life situations (Gall et al., 1998). However, no studies have been published about the influence of alcohol consumption and the corresponding effect on vergence facility. We measured vergence facility following a moderate alcohol intake, which highlighted the deterioration of the ability of the fusional vergence system to change vergence demands. A deterioration in this parameter due to alcohol intake could cause binocular-vision difficulties in real situation, like driving, because our visual system demands constant changes between near and far distances.

Thirdly, another goal of the present study was to use a driving simulator to assess how alcohol consumption deteriorates binocular visual performance and subsequently impairs a highly visual task such as driving. In the present study, the mean speed was higher in the three road sections (dual carriageway, two-lane mountain road, and inner city) with a BrAC of 0.40 mg/l. The greatest increase in mean speed was recorded for the dual carriageway, exceeding the legal driving limit of 120 km/h. In accordance with other studies, mean speed rises for a legal BAC of 0.5 g/l or 0.8 g/l (Mets et al., 2011; Christoforou et al., 2012; Vollrath and Fischer, 2017). Mean speed SD also increased in the three sections following alcohol consumption, indicating increased difficulty in maintaining a constant velocity.

The SDLP is a valid parameter for measuring how much drivers weave across the road after consuming alcohol (Helland et al., 2013). In our study, the SDLP was worse in the dual carriageway and in the two-lane mountain road, which indicates that subjects found it harder to follow road trajectories. Others studies confirmed a higher SDLP with a BAC of 0.5 g/l (Freydier et al., 2014) and 0.8 g/l (Mets et al., 2011; Charlton and Starkey, 2015) (BrACs of 0.25 and 0.40 mg/l, respectively), and for a BrAC above 0.25 mg/l (Casares-Lopez et al., 2020a). In the present study, the distance traveled invading the opposite lane or the distance traveled invading the shoulder significantly increased with a BrAC of 0.40 mg/l. This was congruent with Allen et al who also found that lane deviation increases at a BAC level of 0.55 and 1.1 g/l (BrACs of 0.28 and 0.55 mg/l, respectively), which was explained through lower driver control parameters (Allen et al., 1975; Allen et al., 1996). Moreover, our results confirmed that after consuming alcohol, the greater the inherent difficulty in following the road (the two-lane mountain road with respect to the dual carriageway), the greater the likelihood of crossing lane boundaries, that is, invading the opposite lane or the shoulder. These parameters confirmed that drivers found it harder to control the position of the car in simulated driving under the influence of alcohol.

Another important factor to evaluate during driving is the reaction time (Christoforou et al., 2012), defined as the capacity of the psychomotor reflex to respond in time with respect to a driving situation. In our study, the mean braking reaction times increased significantly between baseline and after consuming alcohol. This indicates that the behavioral reflexes declined with the influence of alcohol. Others studies investigated this parameter with different levels of alcohol (BAC levels of 0.35, 0.4, 0.5, 0.6, 0.8, and 1.1 g/l), and they all reported an increase in reaction time (Allen et al., 1975; Deery and Love, 1996; Banks et al., 2004; Jongen et al., 2014). At a BAC level of 0.8 g/l (equivalent to a BrAC of 0.40 mg/l), Jongen et al obtained a significant increase of 0.209 s in the psychomotor reaction time. They suggested that one of the most common effects of alcohol relevant to potential driving impairment is sedation or drowsiness associated with slower responses and attention deficits (Jongen et al., 2014). Banks et al also established that an increase in electroencephalogram-measured somnolence impaired driving simulator performance in parameters such as reaction time and number of collisions (Banks et al., 2004). Khan and Timney found that the decline in driving performance was due to an impairment in a variety of perceptual and motor systems and the failure to process information correctly (Khan and Timney, 2007). Alcohol can also increase the incidence of distraction-related behaviors, impacting simulated driving performance (Wester et al., 2010). With this in mind, in our study, the mean collision parameter also increased significantly for the BrAC level of 0.40 mg/l (by a factor of 4.3). In all the simulated driving parameters, we measured a BrAC of 0.40 mg/l had a considerable effect on the subjects' behavior, affecting their capacity to drive safely.

Fourthly, we found a correlation between visual deterioration (including fusional reserves, stereoacuity and visual acuity) and simulated driving impairment, revealing that these visual parameters influence driving performance. In this research, the overall visual performance is mainly constituted by fusional vergences and stereoacuity, highlighting the importance of these binocular functions on the simulated driving performance. Stereopsis is considered the most advanced state of binocular vision, contributing to seeing depth (three-dimensional perception). Although stereopsis is usually characterized by maximum disparity (Jimenez et al., 2008b) and stereoacuity, the latter is the main visual function used in clinical practice, and it is sensitive to ocular changes, influencing binocular visual performance (Castro et al., 2018). Therefore, we consider that far stereoacuity could be considered in visual examinations for driving licenses given its widespread use to characterize binocular vision (Owsley and McGwin, 2010), since it could play an essential role in driving safely. It should be taken into consideration that some monocular cues contribute to obtaining information on relative distances and depth in the perceived scene, which seem to be sufficient to meet driving standards and drive safely. In fact, in the absence of binocular vision and stereopsis, driving under monocular viewing conditions is allowed in most countries (International Council of Ophtalmology, 2006). However, it has been demonstrated that an induced deterioration of binocular vision and monocular viewing conditions negatively influences simulated driving (Molina et al., 2021) and monocularity significantly deteriorates driving performance under more demanding conditions, such as car racing (Adrian et al., 2019). . We centered our investigation on driving under normal binocular viewing conditions, the most typical natural conditions, although it would be of interest in future work to study the implications of monocularity on driving performance in challenging conditions like those studied here, i.e., after alcohol intake. Casares-López et al demonstrated that other visual parameters such as contrast sensitivity and retinal straylight have an important impact on simulated driving after consuming alcohol (Casares-Lopez et al., 2020a). However, they stated that the contribution of these two visual variables was limited (16.1%), indicating that other visual functions or psychomotor aspects may also influence driving ability after alcohol consumption. This limitation is also present in our study, although we have more completely analyzed binocular vision through different visual functions, and maintained a stable alcohol content of 0.40 mg/l. However, in further investigation it would be interesting to consider the effects of both visual and psychomotor aspects on driving under the influence of alcohol.

Although subjects were instructed to drive normally and respect the traffic rules just as they would in real life, the study may be limited by the fact that subjects do not interpret risk in the experimental task with the same realism as they do in real-world driving. However, we used a driving simulator because it represents an efficient, applicable, and safe device to assess driving performance (Allen et al., 1975; Allen et al., 1996; Shechtman et al., 2009; Guinosso et al., 2016) in both natural and challenging conditions (such as under the influence alcohol).

Our findings could help provide a better understanding and quantification of the effect of alcohol consumption on binocular visual performance (focusing particularly on the vergence system and stereopsis) with respect to an important everyday task such as driving. This study represents an overview of the influence of alcohol on binocular vision and simulated driving. In fact, it is very remarkable that even a moderate dose of alcohol such as the one employed in this work, which is the legal limit for driving in 45 countries around the world, significantly diminishes binocular vision and driving capacity. This could tragically increase the incidence of traffic accidents. Visual acuity (with a binocular vision of at least 0.5) is commonly used as a visual parameter during tests to obtain a driving license in most countries around the world (International Council of Ophtalmology, 2006; European Council of Optometry and Optics, 2017). In our study, for a BrAC of 0.40 mg/l, the mean binocular visual acuity remained better than 0.5, measured at 1.09. Even with this good level of binocular visual acuity, our results showed a significant impairment in binocular visual performance and driving ability. Therefore, other binocular vision parameters should also be considered for driving license eye tests, such as stereoacuity and a complete vergence exam, to ensure individuals have a safe level of binocular vision.

Further investigation focused on driving performance in people with monocular vision would be of interest. In fact, this particular driving situation could be compared to the normal binocular scenario under various experimental conditions, such as under the influence of alcohol. It could also be of interest to study how motor function and visual deterioration impair driving performance.

6.5. CONCLUSION

The present study analyzes a complete overview involving the vergence system, binocular visual function (by means of the VA and stereoacuity), and driving parameters (mean speed, SDLP, distance traveled invading the opposite lane, reaction time, number of collisions, etc.) in a baseline session and after alcohol consumption. In the binocular vision, we found strong deteriorations at a BrAC of 0.40 mg/l in stereoacuity, fusional reserves (PFV, NFV, and vergence facility), AC/A, Sheard’s criterion at far, and horizontal phoria at distance causing a decrease in visual binocular performance. We also observed a positive correlation between deterioration of binocular vision and impairment on simulated driving performance. In fact, this is the first study that correlates binocular visual deterioration including fusional reserves with simulated driving performance after consuming a moderate amount of alcohol. Our findings suggest that other binocular vision parameters could be considered for driving license tests such as stereoacuity and a complete vergence exam to ensure a safe binocular vision performance. Therefore, the present research shows the importance of a complete binocular vision exam in drivers to provide a more thorough assessment of the visual system. This study also emphasizes the risk reduced vision and driving performance with moderate alcohol consumption. The use of awareness campaigns could help communicate the hazards of alcohol consumption with respect to road and driver safety due to the difficulty of driving when binocular vision is impaired by alcohol intake.

CHAPTER 7

Conclusions

From the thesis presented, the following conclusions can be drawn:

1 Monocularly, retinal image quality deterioration impairs proportionally visual performance for a wide range of simulated degradations levels inducing forward scattering with Bangerter foils and fog filters: the greater the retinal-image degradation, the poorer the visual performance. Specifically, forward scattering negatively affects: contrast threshold (greater impact with glare), straylight and night vision disturbances. Under a wide range of simulated degradations, the night-vision performance correlated well with the retinal-image quality in such a way that the greater the intraocular forward scattering, the poorer the visual discrimination capacity

2 Characterization of different levels disclose that Bangerter foils induce forward scattering comparable to mature to severe cataracts depending of the degree of penalization. Fog filters induced less forward scattering and night vision disturbances than Bangerter foils. Fog filters with the smallest grain size cause a very strong effect of straylight (veil luminance but scattering (OSI) comparable to natural conditions showing the advantage of this measure (straylight) to assess wide-angle scattering. The BPM2 produces forward scattering comparable to an early-stage cataract.

3 The increase of forward scattering induced monocularly by Bangerter foils and BPM2 filter on the dominant eye cause higher interocular differences, which jeopardize overall binocular visual performance. Specifically, the increase of interocular differences in ocular parameters are correlated with decreases in the binocular summation for different visual functions (visual acuity, contrast sensitivity and night visual disturbances) but also with degradations in stereopsis at far, showing that it is important to limit interocular differences to preserve a correct binocular visual performance

4 Under the effect of defocus in combination with control of pupil size, without inducing interocular differences in pupil diameter, binocular summation prevails and increases with higher defocus, larger pupil size (5 mm against 3 mm) and lower contrast induced in visual acuity due to neural factors and not only to optical ones. This finding shows the binocular-summation benefits when maintaining similar monocular conditions, such as pupil size.

5 Under a moderate breath alcohol content of 0.40mg/l, in young healthy people, the complete vergence performance including phorias, fusional reserves (PFV and NFV) , vergence facility, AC/A, and Percival and Sheard's criteria (at far), impaired respect to baseline condition (without any alcohol intake). These degradations are higher at distance than at near causing a decrease in overall binocular visual performance. In addition, stereopsis and visual acuity impair significantly with a moderate alcohol content.

6 Under a moderate breath alcohol content of 0.40mg/l, in young healthy people, driving performance is negatively affected in driving variables such as mean speed, reaction time, standard deviation of the lateral position, distance traveled invading the opposite lane and number of collisions.

7 Binocular visual deteriorations (including stereopsis, fusional reserves and phorias) are correlated positively with simulated driving performance: the greater the deterioration in binocular visual performance, the poorer the simulated driving performance. It is suggested that a complete vergence exam and assessment of stereoacuity could be taken into consideration for driving license tests.

8 The assessment of the binocular visual performance through different functions as studied in the present doctoral thesis is very important to consider since this performance influences daily visual tasks as driving. Even more, these tasks and the binocular visual performance are affected by a moderate alcohol consumption showing a correlation between them.

Future research

Regarding future research, several studies could be of interest to deepen the knowledge of the deterioration of binocular vision. Firstly, following the conclusions of the Chapter 5, a study could assess the neural binocular summation effect using electrophysiological techniques (mainly, pattern visual evoked potential) in young healthy eyes undergoing different levels of defocus under different controlled pupil size conditions. Secondly, another interesting study related to the binocular visual performance and interocular differences could be promoted through the analysis of the influence of a wide range of interocular differences on driving performance with and without alcohol consumption in young healthy people. In addition, regarding driving and visual performance, an investigation could focus on a cohort of young experienced drivers separated in two groups: drivers using only their dominant eye occluding their non-dominant eye to drive (which could be penalized with Bangerter foils to reduce visual acuity) and drivers with normal binocular vision. Therefore, the study would compare both groups in driving performance. Finally, it would be interesting to analyze other commercial filters in monocular and binocular viewing conditions, such as holographic diffusers, since the forward scatter profiles are usually provided by manufacturers, as well as to perform the Halo test using different levels of luminance for the peripheral stimuli.

CAPÍTULO 7

Conclusiones

De la presente tesis doctoral se pueden extraer las siguientes conclusiones:

1 Monocularmente, el deterioro de la calidad de imagen retiniana degrada proporcionalmente el rendimiento visual para diferentes niveles de difusión luminosa intraocular (*intraocular scattering*) inducidos con láminas de Bangerter y filtros de niebla. Cuanto mayor es el deterioro de la imagen retiniana, peor es el rendimiento visual. Concretamente la difusión luminosa intraocular afectó negativamente al umbral de contraste (mayor impacto con deslumbramiento), al velo luminoso y las alteraciones de la visión nocturna. Para los diferentes grados de deterioro, el rendimiento de visión nocturna se correlaciona bien con la calidad de la imagen retiniana de modo que cuanto mayor es la difusión luminosa inducida, peor es la capacidad de discriminación visual en condiciones de baja iluminación.

2 Las láminas de Bangerter usadas habitualmente para tratar la ambliopía inducen diferentes niveles de difusión luminosa intraocular comparables con los niveles obtenidos en cataratas, desde una catarata madura a una severa, dependiendo del nivel de penalización de estas láminas. Los filtros de niebla inducen menos difusión luminosa intraocular y menos alteraciones de la visión nocturna. Sin embargo, los filtros de niebla con una estructura de grano muy pequeño causan un efecto importante de velo luminoso, aunque el índice de difusión luminosa OSI es comparable a las condiciones naturales (sin filtro), mostrando la ventaja de la medida del velo luminoso para evaluar la difusión luminosa de mayor ángulo. El filtro BPM2 produce difusión luminosa comparable a una catarata incipiente.

3 El aumento de la difusión luminosa inducida monocularmente en el ojo dominante genera diferencias interoculares de distinto grado, afectando negativamente al rendimiento visual binocular. Concretamente, el aumento de las diferencias interoculares in los parámetros oculares medidos está correlacionado con una disminución de la sumación binocular para diferentes funciones visuales (agudeza visual, sensibilidad al contraste y alteraciones de la visión nocturna), pero también se correlaciona con una diminución de la estereoagudeza en visión lejana. De este modo se muestra que es

importante limitar las diferencias interoculares con el fin de preservar el rendimiento de la visión binocular.

4 Bajo condiciones de desenfoque en ambos ojos y contralando el tamaño pupilar (sin inducir diferencias interoculares), la sumación binocular se mantiene y mejora a mayor desenfoque, mayor pupila y para contraste más bajo, y esto es debido a factores neuronales, que, en estas condiciones, y para estos niveles de desenfoque, predominan sobre los ópticos. Este resultado muestra los beneficios que se obtienen en la sumación binocular al mantener condiciones monoculares similares, tales como el tamaño pupilar.

5 Para una tasa moderada de alcohol (BrAC de 0,40 mg/l) y para un grupo de jóvenes sanos, el rendimiento del sistema vergencial en visión cercana y lejana, que incluye la evaluación de las forias, las reservas fusionales (vergencias fusionales positivas y negativas), la flexibilidad vergencial, la relación AC/A y los criterios de Sheard y de Percival en visión lejana, se deteriora tras consumo de alcohol. Este deterioro es mayor en visión lejana, lo que resulta en un peor rendimiento visual binocular en estas condiciones. Además, la agudeza visual y la estereopsis empeoran significativamente para esta tasa de alcoholemia.

6 El rendimiento en la conducción, evaluado en un simulador de conducción a través de parámetros como la velocidad media, el tiempo de reacción, la desviación estándar de la posición lateral del vehículo, la distancia recorrida invadiendo el carril contrario y el número de colisiones, se ve afectado de forma negativa para la tasa moderada de alcoholemia de 0,40 mg/l en sujetos jóvenes y sanos.

7 El deterioro de la visión binocular, evaluado a través de la estereopsis y el rendimiento del sistema vergencial, está correlacionado positivamente con la eficiencia en la conducción, de modo que cuanto mayor es el deterioro en el rendimiento visual binocular, peor es la eficiencia de la conducción. Se sugiere que podría ser interesante incluir un examen visual más completo en las pruebas para la obtención del permiso de conducir que incluyan evaluación del sistema vergencial y estereopsis.

8 La evaluación del rendimiento visual binocular a través de diferentes funciones visuales juega un papel importante y debe ser tenido en cuenta ya que este rendimiento influye en tareas visuales cotidianas como la conducción. Además, tanto la visión binocular como la conducción se ven afectadas por un consumo moderado de alcohol y están correlacionadas.

Futuros trabajos

Con respecto a la investigación futura, se han contemplado varios experimentos que serían interesantes para profundizar en el estudio del deterioro de la visión binocular. En primer lugar, tras las conclusiones del Capítulo 5, podría estudiarse el efecto de la sumación binocular neural en ojos jóvenes y sanos usando técnicas de electrofisiología (especialmente potenciales evocados) bajo diferentes niveles de desenfoque y controlando las condiciones para diferentes diámetros pupilares. En segundo lugar, se podría llevar a cabo otro estudio relacionado con la visión binocular y las diferencias interoculares evaluando la influencia de un amplio rango de diferencias interoculares en la conducción con y sin consumo de alcohol en una población joven. Además, con respecto a la conducción y la visión, otro estudio podría centrarse en un grupo de jóvenes conductores experimentados separados en dos grupos: conductores que usen sólo su ojo dominante para conducir (que podría penalizarse con filtros Bangerter para reducir su agudeza visual) y conductores con visión binocular normal. Por tanto, el estudio compararía la habilidad para conducir en ambos grupos. Finalmente, sería interesante analizar otros filtros comerciales en condiciones de visión monocular y binocular, como difusores holográficos, ya que el perfil de *difusión luminosa* de los filtros normalmente los proporciona los fabricantes. También sería interesante estudiar los halos visuales que producen estos filtros usando el halómetro para diferentes niveles de luminancia del estímulo periférico.

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APPENDICES

APPENDIX 1: LIST OF ABBREVIATIONS

AC/A: Accommodative Convergence/Accommodation

ARMD: Age-Related Macular Degeneration

AUDIT: Alcohol Use Disorders Identification Test;

BAC: Blood Alcohol Content or Blood Alcohol Concentration

BAL: Blood Alcohol Level

BF: Bangerter Foil

BPM: Black ProMist

BrAC: Breath Alcohol Content

BS: Binocular Summation

CCD: Charged-Coupled Device

CGT: Contrast Glare Tester

CIE: Commission Internationale d’Éclairage

CSF: Contrast Sensitivity Function

CS: Contrast Sensitivity

CT: Contrast Threshold

DTIOL: Distance Traveled Invading the Opposite Lane

DTIS: Distance Traveled Invading the Shoulder

ECOO: European Council of Optometry and Optics

ES: Engine Stall

ETDRS: Early Treatment Diabetic Retinopathy Study

fMRI: functional Magnetic Resonance Imaging

FV: Fusional Vergence

GISAH: Global Information System on Alcohol and Health

HCDVA: High-Contrast Visual Acuity at Distance

HOA: Higher-Order Aberration

ID: Interocular Difference

IOLs: Intraocular Lenses

LASIK: Laser-assisted In situ Keratomileusis

LCDVA: Low-Contrast Visual Acuity at Distance

LDA: Light Disturbance Analyzer

LDI: Light Disturbance Index

LOCS: Lens Opacities Classification System

LogMAR: Logarithm of the Minimum Angle of Resolution

MS: Mean Speed

MSSD: Mean Speed Standard Deviation

MTF: Modulation Transfer Function

NDT: National Department of Traffic

NFV: Negative Fusional Vergence

ODPDS: Overall Driving Performance Deterioration Score

OIDS: Overall interocular Difference Score

OQAS: Optical Quality Analysis System

OSI: Objective Scatter Index

OVDS: Overall Visual Deterioration Score

PERG: Pattern Electrorretinogram

PFV: Positive Fusional Vergence

PSF: Point Spread Function

PVEP: Pattern Visual Evoked Potential

RT: Reaction time

SA: Stereoacuity

SDLP: Standard Deviation of Lateral Position

SDSP: Standard Deviation of Speed

SM: Signaling Mistake

SR: Strehl Ratio

TDTOL: Total Distance Traveled Outside the Lane

VA: Visual Acuity

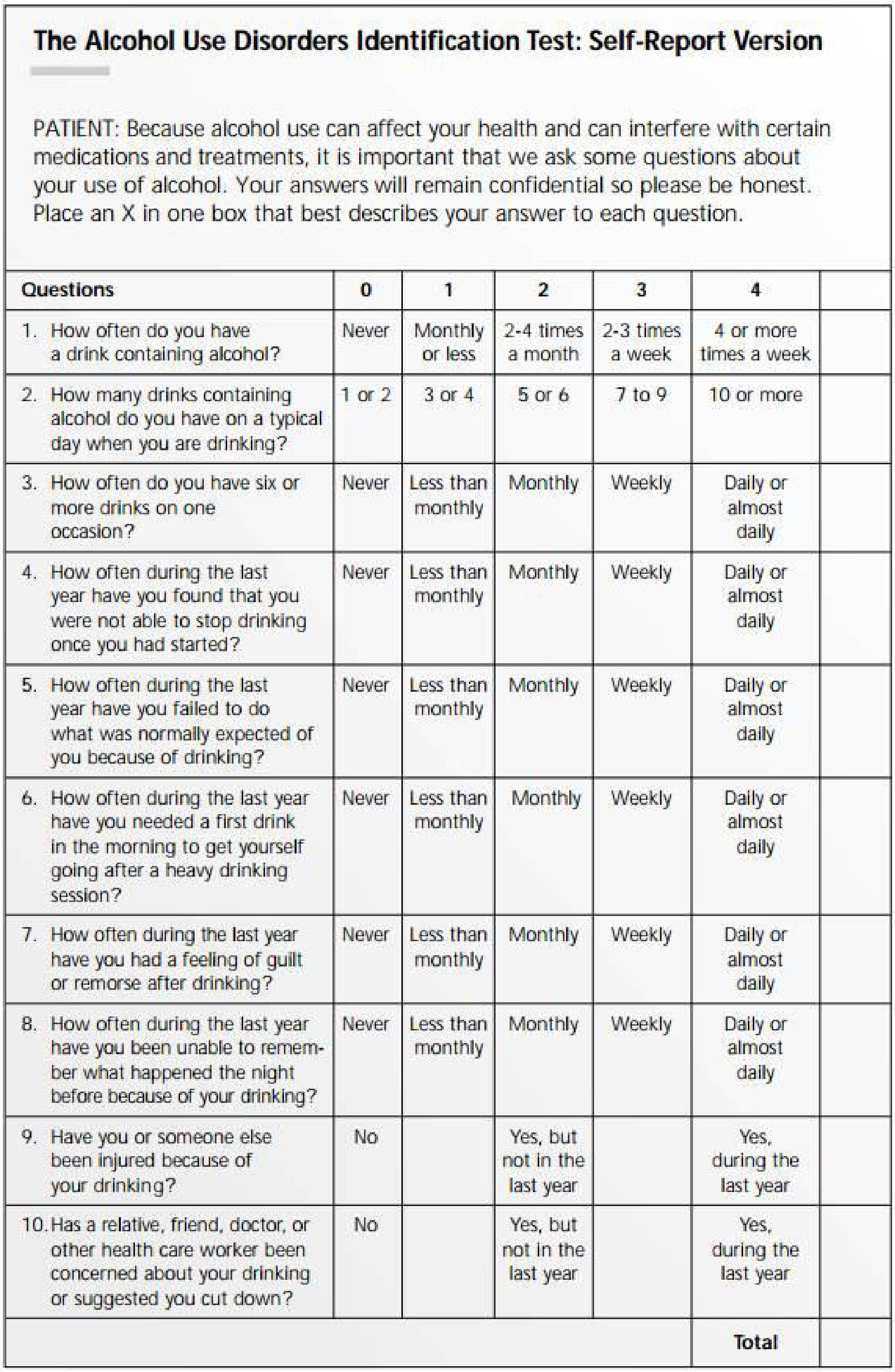
VDI: Visual Disturbance Index

VF: Vergence Facility

VRT: Visual Reaction Time

WHO: World Health Organization

APPENDIX 2: ALCOHOL USE DISORDERS IDENTIFICATION TEST



The Alcohol Use Disorders Identification Test: Self-Report Version

PATIENT: Because alcohol use can affect your health and can interfere with certain medications and treatments, it is important that we ask some questions about your use of alcohol. Your answers will remain confidential so please be honest. Place an X in one box that best describes your answer to each question.

Questions	**0**	**1**	**2**	**3**	**4**	
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times a month	2-3 times a week	4 or more times a week	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more	
3. How often do you have six or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
5. How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
9. Have you or someone else been injured because of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
10. Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?	No		Yes, but not in the last year		Yes, during the last year	
					Total	

RESULTS DISSEMINATION

Scientific Publications generated from the Doctoral Thesis

- Francesco Martino, José J. Castro-Torres, Miriam Casares-López, Sonia Ortiz-Peregrina, Carolina Ortiz, Rosario G. Anera, "Deterioration of binocular vision after alcohol intake influences driving performance". *Scientific reports* 2021. 11, 8904-8904.
  DOI: https://doi.org/10.1038/s41598-021-88435-w

- José J. Castro-Torres, Francesco Martino, Miriam Casares-López, Ortiz-Peregrina, Sonia Ortiz-Peregrina, Carolina Ortiz. "Visual performance after the deterioration of retinal image quality: induced forward scattering using Bangerter foils and fog filters". *Biomedical Optics Express*, 2021, **12**. 2902-2918,
  DOI: https://doi.org/10.1364/BOE.424715

- Francesco Martino, Ana Filipa Pereira-da-Mota, Ana Amorim-de-Sousa, José J. Castro-Torres, José Manuel González-Méijome "Pupil Size Effect on Binocular Summation for Visual Acuity and Light Disturbance" submitted to the journal *Graefe's Archive for Clinical and Experimental Ophthalmology* (under review).

- Francesco Martino, José J. Castro-Torres, Miriam Casares-López, Sonia Ortiz-Peregrina, Carolina Ortiz, José R. Jiménez "Effect of interocular differences on binocular visual performance after inducing forward scattering" submitted to the journal *Ophthalmic and Physiological Optics* (submitted).

Communications in congresses and scientific meeting generated from the Doctoral Thesis

- "Influenza del consumo di alcol su diversi parametri oculari e test visivi". Francesco Martino. University of Napoli "Federico II". Department of Physics "E. Pancini". 2017. Napoli (Italy).

- "Influencia de la ingesta de alcohol en diversos parámetros oculares y test visuales: estudio para dos tasas de alcoholemia". Jornadas de Investigadores y Formación Fomentando la Interdisciplinariedad. 2017. University of Granada (Spain).
- "Alteraciones en la visión nocturna para diferentes tasas de alcoholemia" Miriam Casares-López, José J. Castro-Torres, Francesco Martino, Margarita Soler Fernández, Enrique Hita Villaverde, José R. Jiménez Cuesta. **OPTOM 2018**. Madrid (Spain).

- "Influence of two alcohol intake in night vision" José J. Castro-Torres, Miriam Casares-López, Francesco Martino, Sonia Ortiz-Peregrina, Enrique Hita; José R. Jiménez. **ARVO Annual Meeting 2018**, Honolulu, Hawaii (USA).

- "Efecto de los filtros Bangerter en la calidad óptica ocular y la función visual". José J. Castro-Torres, Francesco Martino, Miriam Casares-López, Margarita Soler Fernández. **XII Reunión nacional de Óptica** (Sociedad Española de Óptica). Castellón de la Plana, del 3 al 6 de julio de 2018.

- "Efecto en la estereopsis del deterioro monocular inducido con filtros". José J. Castro-Torres, Francesco Martino, Miriam Casares-López, Carolina Ortiz y José R. Jiménez. **RNO 2021 - XIII Reunión nacional de Óptica** (Sociedad Española de Óptica), del 22 al 24 de noviembre de 2021.

Research stay:

- Host Center: CEORLAB (Clinical an Experimental Optometry Research Lab). Center of Physics, School of Sciences, University of Minho (Braga, Portugal)
- Supervisor: José Manuel González Méijome.
- Date: from March 18th to June 26th, 2019
- Support: *Convocatoria Erasmus+ de Movilidad Internacional de Estudiantes de Doctorado. Curso Académico 2018-2019* (Erasmus+ Programme for PhD students 2018-2019).

Other scientific activities:

- Participation in the “European Researchers’ Night” ERN (editions 2017, 2018, 2019 and 2021). Place: Paseo del Salón, Granada, Spain:
  - ERN 2017 (Date: 09/29/2017). Activity: «Óptica y Optometría para VER bien».
  - ERN 2018 (Date: 09/28/2018). Activity: «Óptica y Optometría para VER bien».
  - ERN 2019 (Date: 09/27/2019). Activity: «Visión y Optometría: VER para creer… investigando».
  - ERN 2021 (Date: 09/24/2019). Activity: «Visión y Optometría: VER para creer… investigando».