

International Doctoral Thesis / Tesis Doctoral Internacional

**ANALYSIS OF OCULO-VISUAL PARAMETERS AS
BIOMARKERS OF PHYSICAL AND/OR MENTAL
EFFORT**

ÁNALISIS DE PARÁMETROS OCULO-VISUALES
COMO BIOMARCADORES DEL ESFUERZO FÍSICO
Y/O MENTAL



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CERTIFICA:

Que la Tesis Doctoral Titulada “Analysis of oculo-visual parameters as biomarkers of physical and/or mental effort” que presenta D. Jesús Vera Vilchez al superior juicio del Tribunal que designe la Universidad de Granada, ha sido realizada bajo mi dirección durante los años 2013-2016, siendo expresión de la capacidad técnica e interpretativa de su autor en condiciones tan aventajadas que le hacen merecedor del Título de Doctor por la Universidad de Granada, siempre y cuando así lo considere el citado Tribunal.

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En Granada, 25 de Noviembre de 2016



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ABSTRACT

The human eyes are outgrowths of the brain and thus part of the central nervous system (Wilson & O'Donnell, 1988). For this reason, the homeostatic disturbances as consequence of physically or mentally demanding tasks are reflected on different ocular parameters with important implications on the performance of different activities (e.g. sport games, driving), as well as in terms of ocular health (e.g. glaucoma). Due to the fact that the ocular system is tightly linked to the nervous system's activation state, a small number of indices based on the ocular physiology have been used to detect fatigue in several contexts (e.g. military operations, surgical procedures). This field of research has direct applications in sport performance as well as in the management and prevention of ocular diseases, and also has the potential impact to improve operator's performance and patient safety in risky situations. Therefore, it is reasonable to explore the effect of physical and/or mental demands on the oculo-visual system, using objective visual indices sensitive to central nervous system alterations.

The main objectives of the present Doctoral Thesis were to analyze the effects of physical and/or mental effort on the oculo-visual system, and to examine the utility of different ocular physiological indices as neuroergonomic tools for detecting cognitive and physical load and/or fatigue.

To achieve these aims, this research work was divided into three sections where the effect of physical, mental and concomitant physical-mental effort on the visual system was investigated along eight studies. Firstly, the differences in visual function, performance and processing between a group of basketball players and a control group of relatively physically inactive subjects was investigated. Also, we tested the acute and long-term effect of strength training on intraocular pressure in military personnel (Studies I-III). In addition, the effect of mental demanding tasks on different ocular parameters (intraocular pressure, accommodative response, pupil size and ocular aberrations) were assessed in applied (driving) and laboratory contexts (Studies IV-VI). Finally, we measured the effect of the simultaneous performance of physical and mental effort on the visual function and ocular physiology (Studies VII-VIII).

The main findings of this Doctoral Thesis were: I) Basketball players exhibit better performance in several visual capabilities than a control group of relatively physically inactive subjects; II) There is a moderate positive relationship between upper-body strength capabilities and baseline intraocular pressure; III) The performance of strength exercise induces an acute increment in

intraocular pressure, with higher changes when executing bench press in comparison with the squat exercise at the same relative loads; IV) Intraocular pressure is sensitive to the level of mental workload, showing an association between intraocular pressure and nervous system activation state; V) Accommodative response and intraocular pressure decreased as consequence of driver fatigue, and these results represent an innovative step towards an objective, valid, and reliable assessment of fatigue-impaired driving; VI) Astigmatism aberration is sensitive to the level of mental workload, and this effect is maintained when pupils are scaled up to 5 mm. This finding may open up a new possibilities concerning the use of astigmatism aberrations as an indicator of mental load; VII) Performing a dual task (physical/mental) causes an intraocular pressure rise, and increasing the level of mental complexity promotes an additional effect on intraocular pressure variations; and VIII) Simultaneous physical and mental effort alters visual function and eye-hand coordination in different directions (from impairment to enhancement) depending on the level of activation (arousal) and the visual skill tested.

RESUMEN

Los ojos humanos son prolongaciones del cerebro y por lo tanto parte del sistema nervioso central (Wilson & O'Donnell, 1988). Por esta razón, las alteraciones homeostáticas a consecuencia de tareas con demandas físicas o mentales son reflejadas en diferentes parámetros oculares con importantes aplicaciones en el rendimiento de diferentes actividades (e.g. actividades deportivas, conducción), como también en términos de salud ocular (e.g. glaucoma). Debido al hecho de que el sistema ocular está estrechamente relacionado con el estado de activación del sistema nervioso central, un pequeño número de índices basados en la fisiología ocular han sido usados para detectar fatiga en varios contextos (e.g. operaciones militares, procedimientos quirúrgicos). Este campo de investigación tiene una aplicación directa en el rendimiento deportivo, como también en el manejo y prevención de enfermedades oculares, y además tiene un potencial impacto en la mejora del rendimiento del operador y la seguridad del paciente en situaciones de riesgo. Por lo tanto, es razonable explorar el efecto de las demandas físicas y/o mentales en el sistema oculo-visual, usando índices visuales objetivos sensibles a las variaciones del sistema nervioso central.

El principal objetivo de la presente Tesis Doctoral fue analizar los efectos del esfuerzo físico y/o mental en el sistema oculo-visual, y examinar la utilidad de diferentes índices ocular fisiológicos como herramientas neuro-ergonómicas para detectar la carga y/o fatiga física y mental.

Para conseguir estos objetivos, este trabajo de investigación fue dividido en tres secciones donde el efecto del esfuerzo físico, mental y físico-mental concomitante en el sistema visual fue investigado a través de ocho estudios. En primer lugar, las diferencias en la función, rendimiento y procesamiento visual entre un grupo de jugadores de baloncesto y un grupo control de sujetos relativamente inactivos físicamente fue investigado. También, nosotros analizamos el efecto a corto y largo plazo del entrenamiento de fuerza en la presión intraocular en personal militar (Estudios I-III). Además, el efecto de tareas con demanda mental en diferentes parámetros ocular (presión intraocular, respuesta acomodativa, y aberraciones oculares) fue evaluado en contextos aplicados (conducción) y de laboratorio (Estudios IV-VI). Finalmente, nosotros medimos el efecto de la realización de esfuerzo físico y mental de forma simultánea en la función y fisiología ocular (Estudios VII-VIII).

Los principales hallazgos de esta Tesis Doctoral fueron: I) Los jugadores de baloncesto exhiben un mejor rendimiento en varias capacidades visual que un grupo control de sujetos relativamente inactivos físicamente; II) Hay una relación positiva moderada entre las capacidades de fuerza del tren superior y la presión intraocular basal; III) La realización de ejercicio de fuerza induce a un

incremento agudo de la presión intraocular, con mayores cambios con la ejecución del press de banca en comparación con el ejercicio de sentadillas con las mismas cargas relativas; IV) La presión intraocular es sensible al nivel de carga de trabajo mental, mostrando una asociación entre la presión intraocular y el estado de activación del sistema nervioso; V) La respuesta acomodativa y la presión intraocular disminuyen como consecuencia de la fatiga en conducción, y estos resultados representan un paso innovador en la evaluación objetiva, válida y fiable de la fatiga en conducción; V) La aberración astigmática es sensible al nivel de carga de trabajo mental, y este efecto se mantiene cuando las pupilas son escaladas hasta a 5 mm. Este hallazgo puede abrir nuevas posibilidades respecto al uso de la aberración de astigmatismo como un indicador de carga mental; VII) La realización de una tarea dual (física/mental) provoca un aumento de la presión intraocular, e incrementar el nivel de complejidad mental promueve un efecto adicional en las variaciones de la presión intraocular; y VIII) El esfuerzo físico y mental simultáneo altera la función visual y la coordinación ojo-mano en diferentes direcciones (desde el deterioro a la mejora) dependiendo del nivel de activación (arousal) y la habilidad visual analizada.

CHAPTER I. INTRODUCTION

Physical and cognitive load/fatigue: an approximation

In the context of psychology, activation level or arousal is the state of being physiologically alert, awake, and attentive. There is a relationship between arousal and the performance in physical and mental activities. The most famous theory to explain the complex interaction between arousal and performance, known as the inverted U relationship, was first proposed by Yerkes & Dodson (1908) and it was reviewed and extended by Hebb (1955). This theory says that initially performance improves with increased arousal, up to a certain point, after which further increases in arousal produce a performance decrement. This relationship between arousal and performance may be defined as a continuum from extreme sleepiness/physical fatigue to extreme alertness/readiness to engage in physical activity (see **Figure 1**). Due to the fact that different activities require different levels of arousal for optimal performance, it is important to consider that continuous physical and/or cognitive load (time on task) promote fatigue, which contribute to impaired performance (Dickman, 2002). Similarly, task complexity is responsible fatigue, and this can be applied to either physical or mental tasks or a combination of both. Therefore, provided that it is sufficiently long and difficult, the cumulative effect of physical/mental load leads to fatigue.

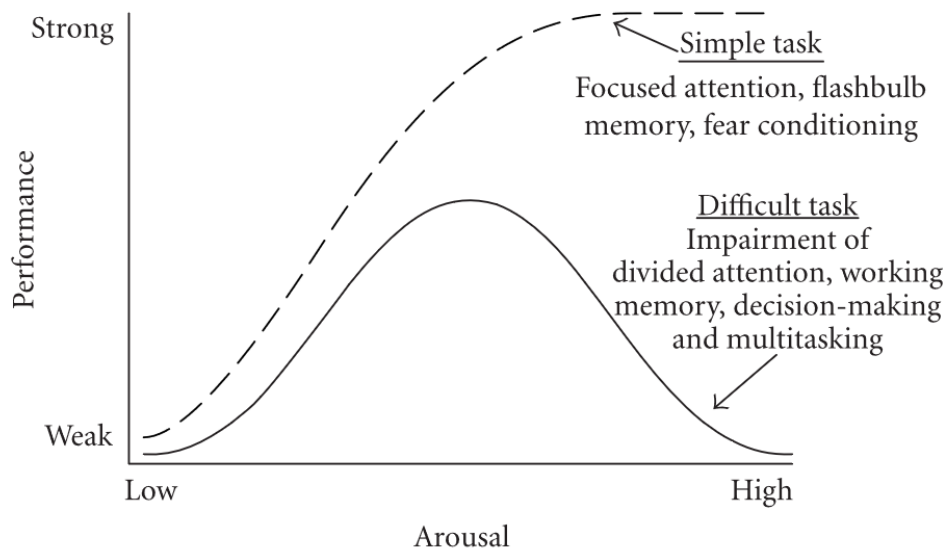


Figure 1. The original version of the Yerkes-Dodson law (Yerkes & Dodson, 1908). This version, based on the actual findings and theorizing of Yerkes and Dodson, takes into account that during simple task (dotted line) the subject can maintain an optimal performance over the entire range of arousal but the complex task (straight line) can be impaired in performance with high arousal levels. Figure 1 is adapted from Figure 2 of Diamond, Campbell, Park, Halonen, & Zoladz (2007).

Body responses to physical and cognitive effort

A great amount of daily activities require cognitive and physical effort (e.g. team sport games, military operations, occupational settings), and those demanding processes can occur separately or simultaneously. To estimate the level of fatigue (physical and/or mental) during tasks is crucial for several reasons. For example, it is important for success in the sports because, among other reasons ratings of perceived exertion and subjective affect generated by the physical activity partially determine the intentions to be physically active in the future (Ekkekakis, Parfitt, & Petruzzello, 2011). Similarly, the effect of fatigue could affect the patient's safety in surgical procedures (Hull et al., 2012) or could degrade neurobehavioral performance and fundamental piloting skills in aviators (Di Stasi, McCamy, et al., 2016) with possible catastrophic consequences. Moreover, researches have focused their attention on physiological indices, which are sensitive to physical and/or mental effort, as potential objective biomarkers of those processes.

When the corporal demands increase by a longer time spent on task or higher task complexity the central nervous system provides a greater supply of resources (Kong et al., 2005). Physiological measures are based on the concept that homeostatic disturbance can be measured by the structures sensitive to those changes (Ryu & Myung, 2005). Cardiorespiratory, musculoenergetic, and hormonal parameters have been demonstrated to be useful indicators of cognitive and/or physical demands (Bray, Graham, Ginis, & Hicks, 2012; Hillman, Erickson, & Kramer, 2008; Hjortskov et al., 2004; Loprinzi, Herod, Cardinal, & Noakes, 2013; Sluiter, Frings-Dresen, Meijman, & Van der Beek, 2000), and changes in the Central Nervous System (CNS) activity have also shown to be significant. For example, Fontes et al. (2013) have recently used functional Magnetic Resonance Imaging (fMRI) to identify brain areas in which activation correlates with increasing degrees of effort in dynamic whole-body exercise, whilst Di Stasi et al. (2015) have investigated how task complexity modulates electroencephalographic activity in pilots during real flight.

Relationship between ocular physiology and physical/mental effort

Considering that the eyes originated as outgrowths of the brain and are therefore considered part of the CNS (Di Stasi et al., 2012; Wilson & O'Donnell, 1988), numerous research has focused its attention on ocular variables as potential objective biomarkers of cognitive and physical processes. In this area, pupil size has demonstrated to be sensitive to manipulations of cognitive and physiological arousal, mediated from the projection of the superior colliculus (Hayashi, Someya, & Fukuba, 2010; Klingner, Tversky, & Hanrahan, 2011; Wang & Munoz, 2015). Similarly, ocular saccadic dynamics have been used to assess cognitive impairments. For example, Di Stasi et al. (2010) found that saccadic peak velocity is affected by variations of mental workload, and also proved the utility of saccadic velocity changes to indicate variations in sympathetic nervous system activation in naturalistic tasks (Di Stasi, Catena, Cañas, Macknik, & Martinez-Conde, 2013). Also, intraocular pressure (IOP) changes as a consequence of exercise and cognitive stressors have been reported, but regarding physical effort, the conclusions were scarce and inconsistent (McMonnies, 2016; Risner et al., 2009). However, autonomic effects (arousal alterations) due to psychological stressors (i.e. mental arithmetic tasks or psychosocial stress) and induced-fatigue tasks alters IOP (Brody, Erb, Veit, & Rau, 1999; Sauerborn, Schmitz, Franzen, & Florin, 1992; Vera et al., 2016; Yamamoto et al., 2008). Interestingly, accommodation variations as a consequence of cognitive tasks may arise at the level of activation state (Davies, Wolffsohn, & Gilmartin, 2005; Saito, Sotoyama, Saito, & Taptagaporn, 1994; Schor, Lott, Pope, & Graham, 1999; Vera et al., 2016).

In the present International Doctoral Thesis, we have focused our attention on several ocular physiological indices such as IOP, accommodative response, ocular aberrations and pupil size, which are detailed below.

Intraocular Pressure (IOP). Segen (2006) defines the IOP as the pressure exerted against the outer layers of the eyeball by its contents. This pressure is determined by the volume of aqueous humour, vitreous and blood within the eye exerting an outward pressure, scleral compliance and extraocular muscle tone exerting inward pressure. The major controlling influence on intraocular pressure is the dynamic balance between aqueous humour production in the ciliary body and its elimination via the trabecular meshwork and the canal of Schlemm (see **Figure 2**). Some pressure sensitive feedback control system may be operative to maintain constant intraocular pressure and the autonomic nervous system, through the sympathetic-adrenal system, plays a crucial role in aqueous humour inflow and outflow (Gherghel, Hosking, & Orgül, 2004). This ocular pressure is measured using a procedure called tonometry, being normal IOP ranges from 10-21 mm Hg. IOP

must be maintained within this normal range to ensure constant corneal curvature and a proper refracting index of the eye. Usually, the higher the pressure, the more risk to the optic nerve. A person with elevated IOP is referred to as a glaucoma suspect, because of the concern that the elevated eye pressure might lead to glaucoma (Skalicky, 2016). An appropriate control of IOP levels is critical in the prevention and reduction of glaucoma, where IOP reduction or stabilization is the only proven method for glaucoma management (Zhao et al., 2016).

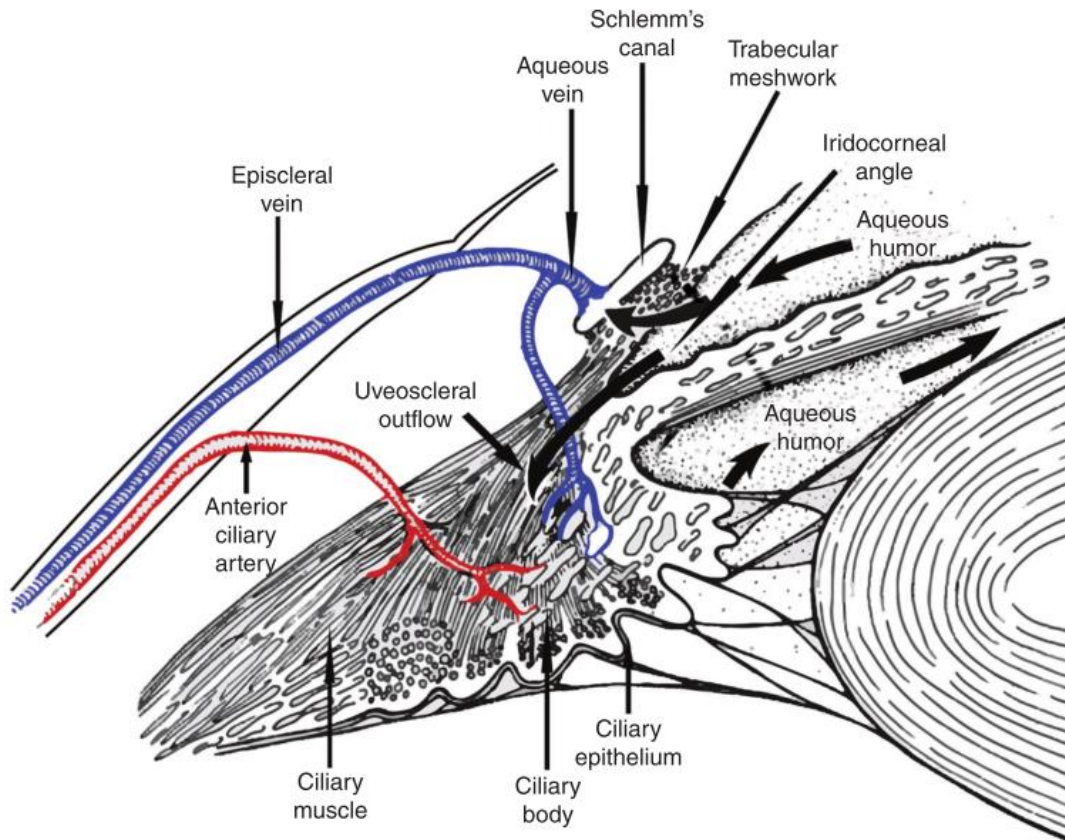


Figure 2. Schematic illustration of the structures involved with aqueous humour formation and outflow. Figure 2 is retrieved from figure 23 of McDougal & Gamlin (2015).

Accommodative Response: Accommodation is the ability of the eye to change the refractive power of the lens and automatically focus objects at various distances on the retina. This mechanism is controlled by the action of the ciliary muscle which is innervated by the autonomic nervous system. There is evidence that autonomic control of accommodation is predominantly parasympathetic and also the sympathetic nervous system produces a small inhibitory action (Gilmartin, 1986). Accommodative response is a static measurement of accommodation and it could be defined by the amount of dioptric adjustment of the crystalline lens of the eye that allows to optimize image quality at different distances (Keeney, Fratekko &, Hagman, 1995). These steady state errors form an intrinsic part of the accommodative control system and are of two types: over-accommodation for far targets, known as "lead" of accommodation, and under-

accommodation for near targets, known as "lag" of accommodation (Charman, 1995) (**Figure 3**). This response can be estimated with reliable and valid objective refraction tool for general optometric practice and research (Sheppard & Davies, 2010).

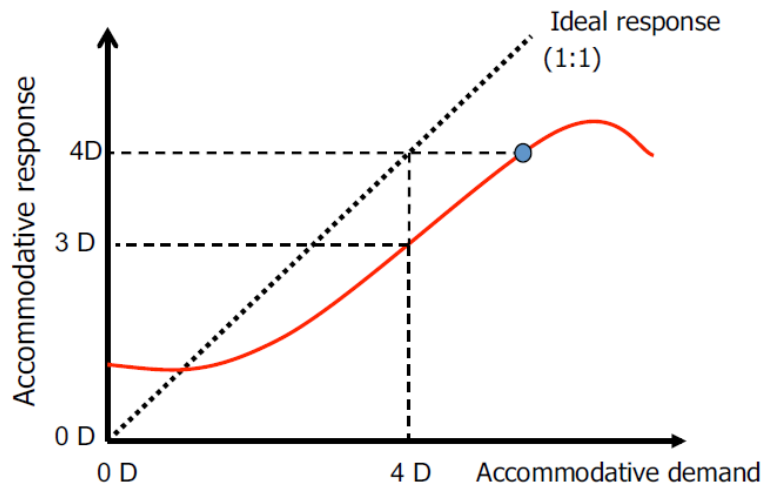


Figure 3. Representation of accommodative response curve as a function of accommodative demand. The dotted line represents the ideal response, and the red line shows a classic accommodative response in general population, indicating a lag of accommodation. Figure 3 is retrieved from figure 1 of López-Gil et al. (2013).

Pupil Size: It could be defined as the aperture of the iris where light can pass through the eye. Pupil size depends mainly on the adapting luminance among other factors such as age, field size, stimuli characteristics, viewing distance or autonomic innervation. The sympathetic branch induces mydriasis (pupil dilatation) and the parasympathetic input produces miosis (pupil constriction) (Neuhuber & Schrödl, 2011).

Accommodation, like pupil size, is controlled by the autonomous nervous system, predominantly mediated by the parasympathetic branch. However, there is anatomical, pharmacological and physiological evidence for an additional sympathetic input via adrenoceptors (Gilmartin, 1998; Winn, Culhane, Gilmartin, & Strang, 2002). Additionally, the role of the autonomic nervous system (both sympathetic and parasympathetic division) in the regulation of intraocular pressure is also well recognized (Lanigan, Clark, & Hill, 1989). As indicated above, these three physiological parameters are modulated by mental workload, and therefore it would be plausible to find a new objective parameter that includes such variations and reflects any change in nervous autonomic balance. In this way, we think in higher ocular aberrations, which have been demonstrated to be sensitive to pupil size and accommodation, and so not so clear to intraocular pressure (Asejczyk-Widlicka & Pierscionek, 2007; Mierdel, Krinke, Pollack, & Spoerl, 2004; Wang, Zhao, Jin, Niu, & Zuo, 2003).

Ocular Aberrations: These reflect the ocular optical quality based on the ocular elements such as the anterior and posterior corneal surfaces, the crystalline lens, and the aqueous and vitreous

humor. Ocular aberrations refer to the deviation of a wavefront exiting the pupil after progressing the optics of the tested eye when compared to a reference wavefront that is aberration free (**Figure 4**). These imperfections in the optics of the eye are measured by aberrometer (wavefront sensor) and expressed as wave aberration errors. The wave aberration is usually defined mathematically by a series of Zernike polynomials. Zernike polynomials are used to classify and represent optical aberrations because they consist of terms of same form as the types of aberrations observed when describing the optical properties of the eye, and can be used reciprocally with no misunderstanding. Moreover, the advantage of describing ocular aberrations using the normalized Zernike expansion, generally depicted as a pyramid, is that the value of each mode represents the root mean square (RMS) wavefront error attributable to that mode. Coefficients with a higher value identify the modes (aberrations) that have the greatest impact on the overall RMS wavefront error in the eye and thus in reducing the optical performance of the eye. Second-order Zernike terms represent lower order aberrations, the conventional aberrations defocus (myopia, hyperopia and astigmatism) correctible with glasses, contact lenses and refractive surgery. Lower order aberrations make up about 85 per cent of all aberrations in the eye. Higher order aberrations is a term used to describe Zernike aberrations above second-order. Third-order Zernike terms are coma and trefoil. Fourth order Zernike terms include spherical aberration, and so on. Higher order aberrations make up about 15 percent of the overall number of aberrations in an eye (Thibos, Applegate, Schwiegerling, & Webb, 2002).

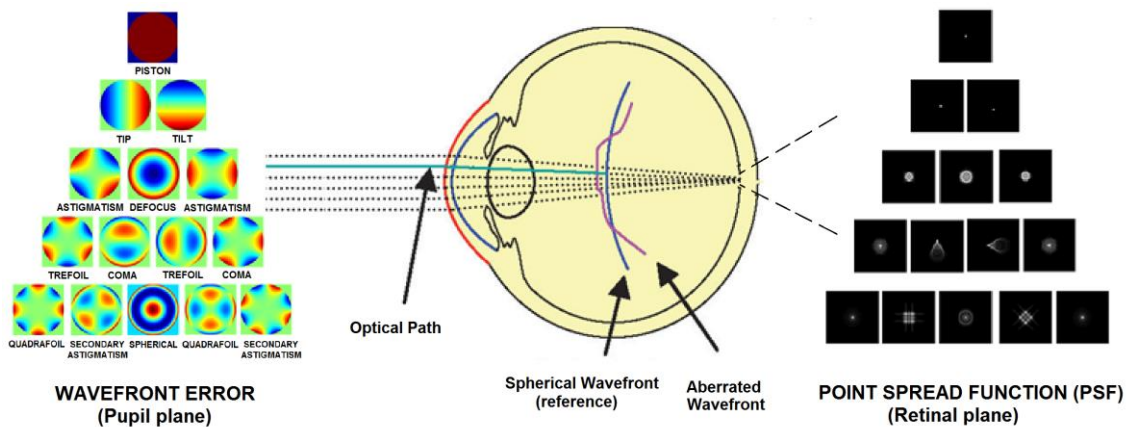


Figure 4. Representation of ocular aberrations formation, showing the first 15 Zernike terms and their corresponding far field point spread functions (PSF). Figure 4 is adapted from figure 3 of Vera-Díaz & Doble (2012) and figure 5 of Einigamner, Oltrup, Bende, & Jean (2009).

Justification of the present doctoral thesis

This line of research began with the intention of achieving a multidisciplinary approach to understanding the relationship between physiological alterations and the visual system, mainly in the context of sport. We conducted an extensive literature search, which led us to realize the importance of collaborating with experts from different fields of research related to this area.

Nowadays, nobody questions the effect of corporal adaptive processes in ocular function but interest in this topic for a substantial number of researchers is relatively recent. A few years ago, several authors focused their attention on the influence of physiological changes resulting from diverse causes (e.g. circadian variations, alcohol consumption, cannabinoids intake, etc.) on ocular health (Campbell, Doughty, Heron, & Ackerley, 2001; Flom, Adams, & Jones, 1975; Gherghel et al., 2004; Green, 1998; Liu et al., 1998; Miller, Pigion, & Takahama, 1986; Wegner & Fahle, 1999). However, the interest in short and long term effects of physiological alterations in the visual system from different activities, which include physical and/or mental processes (e.g. physical exercise, military operations, surgical procedures, driving, etc.) has grown in recent years (Di Stasi et al., 2010; Di Stasi et al., 2014; Fortes et al., 2011; Risner et al., 2009; Vera et al., 2016). These questions have been investigated by some authors in the past but the approach to this problem was addressed unilaterally, that is, eye specialists underestimated the role of the physical or cognitive effort to induce physiological changes, and similarly, sport researchers and psychologists did not pay enough attention to the ocular measures as possible factors to be considered. We are convinced that the main strength of this work lies in the multidisciplinary nature of the researchers' group, which guarantees a holistic approach to the issue and specialized analysis by experts in each discipline.

Our first steps with the research group "Structures and processes involved in interactive sports" allowed us to understand that, whilst the physical demands of sports are obvious, cognitive effort is also necessary to success. Thus, physical and mental aspects should be considered, particularly in interactive sports, where decision making plays a fundamental role.

At this point, we decided to investigate the influence of mental and physical effort in oculo-visual parameters. This new line of research was divided in three topics, as explained above: the ocular physiological response to different types of physical demands, the effect of cognitive demand on ocular functioning, and lastly, the effect of simultaneous physical and mental effort on oculo-visual indices. We aimed to test the effect of those demands on the ocular system but we also hoped to explore the possibility of using ocular biomarkers as indices of physical and/or mental

effort (load and/or fatigue), taking advantage of this two-way relationship between the ocular system and nervous system's activation state.

The first three studies focused on the association between sport and the oculo-visual system. As a first step, we investigated the differences in visual function, performance and processing parameters between a group of basketball players and a group of sedentary individuals. Secondly, we aimed to test the both chronic and acute effect of physical fatigue on the ocular physiology. Previous studies of this type were mainly interested in the effect of dynamic exercise, using low impact aerobic exercise, on intraocular pressure. However, little work had been conducted into the effect of strength training, which is very popular nowadays. Thus, we analyzed the relationship between strength capabilities, using force-velocity parameters for the ballistic bench press exercise, and baseline intraocular pressure values. Finally, the third study was designed to investigate the immediate consequence of strength training at different intensities on intraocular pressure.

The next three experiments were designed to check the effect of cognitive processing on ocular indices. In the fourth study, we investigated the sensibility of intraocular pressure to mental task complexity manipulation in a laboratory setting, and we used heart rate variability to validate it. With the fifth study we tried to go a little bit further by using a context closer to the real world (driving simulator), in this case we incorporated an additional objective ocular index such as binocular accommodative response. In response to our previous findings, we aimed to ascertain a novel ocular parameter, which is sensitive to the ocular physiological changes (e.g. intraocular pressure, accommodative response, pupil size) previously found as consequence of mental effort. This candidate index to capture the effect of cognitive processing was ocular aberrations in terms of the root mean square (RMS) wavefront error.

To address our initial research question, we combined simultaneous physical and cognitive demands to test the effect of dual tasks in the oculo-visual system in our experimental designs. As we stated above, both requirements are necessary to success in sport and this assumption has been well established in the field of sport science and sport psychology during the last few years. Due to the fact that ecological settings do not permit an exhaustive control of external factors, we decided to begin this line of research under well-controlled laboratory conditions with the intention of applying our work to real contexts in future studies. To do this, we conducted the seventh and eighth studies. These experiments permitted us to assess the effect of a dual physical/mental task on oculo-visual parameters, the seventh study being focused on oculo-physiological indices, and intraocular pressure, while with the last, we evaluated how visual function is altered during those type of tasks.

CHAPTER II: OBJECTIVES

The main objective of the present International Doctoral Thesis was to analyze the effects of physical and/or mental effort on the oculo-visual system. Moreover, the effects of physical and mental tasks on visual function and performance, as well as to test the utility of ocular physiological indices as a tool for monitoring cognitive and physical load and/or fatigue. The outcome of this Doctoral Thesis is divided in three sections and eight studies.

- 1. Physical effort.** We aimed to investigate the visual differences between athletes and sedentary individuals, and also to test the effect of strength training on intraocular pressure.
 - 1.1 To investigate the differences in accommodative and binocular function, visual performance, and processing between semi-professional basketball players and individuals without sport background.
 - 1.2 To determine the relationship between the maximal mechanical capabilities of the body-upper muscles to generate force, velocity and power with baseline intraocular pressure.
 - 1.3 To examine the effect of the intensity (%RM) of strength exercise on IOP and compare IOP variations between the ballistic bench press and jump squat exercises for the same relative loads.

- 2. Mental effort.** To assess the influence of cognitive effort on ocular physiology in laboratory and applied settings (driving). We aimed to highlight the effect of mental tasks on intraocular pressure and accommodative response, as well as ocular aberrations, and explore the use of these as indicators of mental load and fatigue.
 - 2.1 In a laboratory setting, we aimed to investigate the effect of mental workload complexity (high/low) on intraocular pressure, using heart rate variability and subjective perceived mental load as control indices.
 - 2.2 To assess the influence of driving fatigue in accommodative response and intraocular pressure with the aim of using these ocular indices (accommodative response and intraocular pressure) as a valid instrument to detect driving fatigue.
 - 2.3 To search for a new ocular marker (ocular aberrations) of the level of mental workload based on the optical quality and dependent of the previous ocular parameters investigated in the current thesis.

3. Concomitant mental and physical effort. To assess the influence of overlapping physical and mental demands on ocular indices. We tested how concomitant physical and cognitive demands affect the ocular physiology and visual function.

3.1 To test IOP changes after a bout of moderate continuous exercise, and whether this potential effect is modulated by the concomitant presence of high or low cognitive demands. Also, to try and ascertain whether IOP, measured before exercise, can predict the impact of physical exercise, with high or low cognitive demands, in subjective assessments of effort intensity and affective valuation of such effort.

3.2 To assess the influence of concomitant resistance exercise and mental workload, with two different levels of cognitive demand (high and low), on accommodative, binocular, and oculomotor function.

CHAPTER III: PHYSICAL LOAD AND FATIGUE

Study 1. Basketball players present better visual abilities than sedentary individuals

Introduction

Athletes need to gather a great amount of information, mainly visual, swiftly from the environment in order to execute appropriate motor tasks (Babu, Lillakas, & Irving, 2005). There is evidence that athletes develop peculiar mechanisms of occipital neural synchronization during visuo-spatial demands, showing better visuo-motor performance compared to non-athletes (Del Percio et al., 2007). Previous studies tend to indicate that athletes present better visual skills than do sedentary individuals but this issue is far from being settled (Barrett, 2009). Several studies questioned whether visual skills in athletes are innate or they are improved with systematic sport practice (Ludeke & Ferreira, 2003). In this context, it has been established that constant practice and sports vision training programs help to improved certain visual abilities, while the innate contributions seem to be insignificant (Quevedo-Junyent, Aznar-Casanova, Merindano-Encina, Cardona, & Solé-Fortó, 2011; Schwab & Memmert, 2012).

Previous investigation suggests that particular sets of visual skills are sport-dependent because each discipline has differing visual needs and demands (Laby, Kirschen, & Pantall, 2011). The visual information during basketball, as a dynamic sport, comes from the position of the ball and player. Thus, basic visual function based on good optical quality, oculomotor coordination, binocular, and accommodative function or stereopsis are crucial to success in ball games, and particularly in basketball (Sillero, Refoyo, Lorenzo, & Sampedro, 2007). In addition, player's performance depends on the cognitive capabilities and the visuo-motor reaction times (Kioumourtzoglou, Kourtesses, Michalopoulou, & Derri, 1998).

Nevertheless, it is not clarified if athletes' superiority is due to basic visual function or perceptual and cognitive skills (Ryu, Abernethy, Mann, Poolton, & Gorman, 2013). Although, the increasing body of knowledge supports a multidimensional approach, considering visual, perceptual and cognitive factors to characterize expertise (Ward & Williams, 2003b). Some studies concluded that athletes possess better visual function than sedentary individuals (Ciuffreda & Wang, 2004). However, scarce investigations use an extended optometric test battery in a specific sport discipline, and thus no solid conclusions have been obtained to date. For example, differences between professional volleyball players and a control group have been stated for saccadic eye

movements and facility of ocular accommodation (Jafarzadehpur, Aazami, & Bolouri, 2007), as well as a better near stereoacuity in youth baseball/softball players in comparison to non-ball players (Boden, Rosengren, Martin, & Boden, 2009). By contrast, Paulus et al., (2014) found that soccer players had stereopsis similar to that of individuals without a soccer background. On the other hand, visual information processing also plays a fundamental role in sport performance, permitting a precise decision making process in a certain time (Mangine et al., 2014). Several studies have shown that athletes have an improved ability to track a moving target, peripheral awareness, and a different strategy in the treatment of visual information, among others, than do non-athletes or less experienced players (Alves, Spaniol, & Erichsen, 2014; Quevedo-Junyent et al., 2011; Uchida, Kudoh, Murakami, Honda, & Kitazawa, 2012). Specifically in a recent study, Mangine et al., (2014) found a relationship between faster visual tracking speed and better basketball-specific performance in NBA players.

Considering the previous literature and the ongoing debate concerning to the differences in visual function and perceptual abilities between athletes and sedentary population, we investigate the basic visual function and perceptual visual skills in a specific sport discipline, basketball in our case, and it may incorporate more knowledge in this aspect. Therefore, in the present work, we tested several parameters related to the basic visual function such as accommodative response, near point of convergence, near and far fusional vergences, and near and far stereoacuity. Regarding to perceptual abilities, we also assessed visual performance by visual-discrimination capacity, and visual information processing by visual reaction time and eye-hand coordination. To check the differences in basketball practice involvement between athletes and individuals without sport background, we measured heart rate variability at rest and obtained subjective report data. We hypothesized that inherent visual involvement during systemic basketball practice can exert an improvement in both basic visual function and perceptual visual parameters mainly involved. The answer to our research question can have theoretical and practical consequences for basketball performance and training protocols.

Methods

Participants and ethical approval

The study included a total of 33 male university students, of which 18 belonged to different basketball teams in a regional league and 15 had no history of sporting activity (mean age \pm s: 23.28 ± 2.37 , and 22.27 ± 2.09 , respectively) (**Table 1**). This study was conducted abiding by the Code of Ethics of the World Medical Association (Declaration of Helsinki) and permission was

provided by the university Institutional Review Board (IRB). All volunteers signed an informed consent form prior to the study.

Admission criteria included: a) being healthy; b) ≥ 6 hours of moderate exercise per week for the athletes group, and ≤ 1 hours of exercise per week for the non-athletes group; c) not presenting any ocular pathology; d) not taking any medication, e) presenting static monocular (in both eyes) and binocular VA ≤ 0 log MAR ($\geq 20/20$); f) having a corrected refractive error ≤ 3.5 D for myopia and hyperopia and ≤ 1.5 D of astigmatism and being contact lenses wearers; and g) scoring less than 25 on the Conlon Survey (Conlon, Lovegrove, Chekaluk, & Pattison, 1999), which assesses visual discomfort, and less than 21 at the CISS (Convergence Insufficiency Symptom Survey) (Horwood, Toor, & Riddell, 2014) (see **Table 1**). All participants were instructed to avoid alcohol consumption and vigorous exercise 24 h before the experimental session, to sleep for at least 7 h, not to consume caffeine beverages or other stimulants in the 3 h prior to testing, and to follow the regular diet but not to eat 2h prior to testing.

Table 1. Anthropometrical and visual characteristics, and visual symptomatology of the 33 participants included in this study by groups.

Sample characteristics	Basketball players (n=18)	Sedentary subjects (n=15)
	M \pm s, range	M \pm s, range
Height (cm)	177.17 \pm 7.26, 167-191	181.8 \pm 4.97, 173-190
Weight (Kg)	71.85 \pm 7.48, 62-88	75.87 \pm 10.35, 60-95
Visual Acuity (log MAR)	-0.14 \pm 0.08, -0.2-0	-0.15 \pm 0.06, -0.2, 0
Spherical refractive error (D)	-0.25 \pm 0.8, -3.375-0	-1.01 \pm 1.43, -3.5-0
Astigmatism (D)	0.03 \pm 0.12, 0-0.5	0.32 \pm 0.43, 0-1.13
Subjective measures		
CONLON	5.77 \pm 4.25, 0-17	7.47 \pm 5.74, 0-19
CISS	6.11 \pm 4.19, 0-16	8.47 \pm 5.82, 0-19

Test procedures and materials

Heart-rate variability measure and analysis

To ensure physical involvement differences, we measured heart-rate variability (HRV) (Pumprla, Howorka, Groves, Chester, & Nolan, 2002). A number of studies have concluded that endurance training enhances vagal tone in athletes, which may contribute in part to lower the resting heart rate (Aubert, Seps, & Beckers, 2003). Thus, before the visual examination, the participant was asked to lie in a supine position in a quiet room for 6 min. The heart rate was monitored by using a Polar RS800CX wrist device (Polar Electro Oy, Kempele, Finland), set to measure both the heart rate (HR) and heart-rate variability (HRV). The time series of HRV was taken from the electrocardiogram, identifying the occurrence of each R wave (belonging to the QRS complex) and calculating the time lapse between two consecutive R waves (see Acharya, Joseph, Kannathal, Lim, & Suri, 2006). Subsequently, the data were transferred to the Polar ProTrainer Software and each downloaded R-R interval (inter-beat R wave to R wave) file was then further analysed using the Kubios HRV Analysis Software 2.0 (The Biomedical Signal and Medical Imaging Analysis Group, Department of Applied Physics, University of Kuopio, Finland) (Tarvainen, Niskanen, Lipponen, Ranta-Aho, & Karjalainen, 2014). R-R intervals which differed more than 25% from the previous and subsequent R-R intervals were excluded. Those removed R-R intervals were replaced by conventional spline interpolation so that the length of the data did not change. In this study, the parameters used to analyse HRV within the time domain were the mean R-R interval (RRi), and the root-mean-square difference of successive normal R-R intervals (rMSSD).

Ocular and visual examination

Ocular parameters related to ocular refraction, accommodative and binocular function, visual performance, and visual information processing were examined. All tests were conducted under photopic illuminance conditions (mean value \pm s: 152.4 ± 2.45 lux), with the exception of visual-discrimination in scotopic illuminance conditions (~ 0 lux), which were quantified in the corneal plane with an illuminance meter T-10 (Konica Minolta, Inc., Japan).

Ocular refraction

Monocular and binocular visual acuity (VA) was determined using a computerized monitor with the logarithmic letters chart test employing the Bailey-Lovie design (VistaVision, Torino, Italy) at a distance of 5 m.

Ocular refraction consisted of an objective refraction with non-cycloplegic retinoscopy while the participant maintained a fixed gaze on a distant non-accommodative target, and finally each participant underwent a full monocular and binocular subjective refraction, using an endpoint criterion of maximum plus consistent with best vision.

Accommodation, binocular, and oculomotor parameters

All tests were conducted with the best correction following the recommendations given by Scheiman & Wick (2008).

The accommodative response, measured by the monocular estimate method (MEM) retinoscopy, was carried out by very briefly interposing, in front of one eye at a time, convergent or divergent lenses until neutralizing the reflex found in the horizontal meridian, while the participant read a test close-up with 0.18 log MAR (20/30) letters.

The near point of convergence was evaluated by the push-up technique using an accommodative target. A 0.18 log MAR (20/30) single letter on the fixation stick was used as the target. The target was moved closer until the participant experienced constant diplopia on the stick (breakpoint). Then we asked the patient to move it away from the eye until single vision was restored (recovery point).

Near and distance negative and positive vergence amplitude were measured. The negative fusional vergence was measured first to avoid affecting the vergence-recovery value because of excessive stimulation of convergence. A gradually increasing prism bar was introduced in the dominant eye while the patient fixed the gaze on a column of the Snellen optotype, corresponding to the highest VA at 40 cm and 6 m fixation, respectively. When the prism caused the patient to experience double vision, the amount of prism (breakpoint) was recorded. The prism power was then reduced until the double images could be fused again (recovery point).

Static far stereo acuity was tested using the Stereo D6/D8 (VistaVision, Torino, Italy) at 5 m distance away using a polarizing viewer. This test presents a range from a maximum of 300 seconds of arc to a minimum of 10 seconds of arc and only one circle from 5 possible choices had crossed disparity. The participant was asked to identify which circle seemed to be at a different distance with respect to the other two (at near) or four (at distance). Static near stereo acuity was measured using the Randot Stereotest Circles (Stereo Optical Company, Chicago, IL, USA) at a distance of 40 cm. Within each of 10 targets there were 3 circles. This test presents a range from a maximum of 400 seconds of arc to a minimum of 20 seconds of arc. The level of stereo acuity was recorded as the last series of targets correctly answered.

To test facility of accommodation, the Hart chart was read under binocular conditions. This procedure presents blur and vergence-related visual feedback and function in interactive manner (Vasudevan, Ciuffreda, & Ludlam, 2009). Participants were instructed to alternatively read one letter from the distance Hart chart (5 m) in primary position, and then shift their focus to the near Hart chart (40 cm) placed 30° inferiorly, and so forth across the lines of letters as rapidly as possible. The number of cycles completed in 60 seconds were determined, as well as the number of errors made.

Visual performance

We evaluated the visual-discrimination capacity, quantifying the visual disturbances perceived by the participant using a visual test conducted by the software Halo v1.0 (Castro, Pozo, Rubiño, Anera, & Jiménez Del Barco, 2014). The participant's task consisted of detecting luminous peripheral stimuli around a central high-luminance stimulus over a dark background. All of the stimuli were achromatic. The distance from the observer to the test monitor (1280 x 1024 LCD screen) was 2.5 m and the test was performed binocularly. The size of the stimulus was 39 pixels for the radius of the central stimulus and 1 pixel for the peripheral one, subtending 0.61 and 0.02 deg, respectively, from observer's position. The monitor showed 72 peripheral stimuli around the central one, distributed along 18 semiaxes. Each of the 72 stimuli was presented twice. After a 3-min adaption period to darkness of the monitor background, there was 1 min adaptation to the main stimulus, and then the participant was randomly presented with peripheral stimuli around the central stimulus. The participant, on detecting peripheral spots, pressed a button on the mouse, storing this information for subsequent treatment and calculation of the visual disturbance index (VDI) after the test was concluded. The VDI takes values from 0 to 1. The greater value indicates a greater contribution of visual disturbances, such as glare or visual halos around the luminous stimuli, and therefore poorer discrimination capacity.

Visual-information processing

The Wayne Saccadic fixator (Wayne Engineering, Skokie, IL, USA) was used for evaluating visual reaction time. This apparatus consists of a 29-inch square panel containing 33 red lights switches. A computer chip generates a variety of patterns of light to which an individual responds by pushing the lighted switch to extinguish the light. A great variety of display patterns, speed, and situations can be programmed. The "Sports Vision Release/Locate Reaction Time" program was chosen to test visual reaction time and performed three times after familiarization. The test instructions consisted of pressing the start/reset button, holding button depressed until a signal is heard (liberalization time), releasing the button and pressing the illuminated light/button on the saccadic fixator (localization time). Just one light was used and appeared in a random position each time. Two scores were given to each trial, for the time of liberalization and location (milliseconds) (Abernethy & Wood, 2001; Vogel & Hale, 1990).

To test eye-hand coordination, we used a standardized test developed by Dr. Jack Gardner (Wayne Engineering, Skokie, IL, USA) with the Wayne Saccadic Fixator, which takes jointly the proaction (time period in which each light stays lit until the button is pressed) and reaction times (preset amount of time in which each light stays lit before automatically switching to another light regardless of whether the button is pressed) into account for accurate and repeatable rapid testing. The lights start moving automatically at the preset speed (60 lights per min). For each correct

response, the speed increases. At the end of the preset time (30 sec), the display shows the number of correct responses, the average speed, and the final speed in lights/min. The score was the product of number of lights scored and the final speed of presentation of the lights (Vogel & Hale, 1990).

A mean of three measurements was obtained in M.E.M, near point of convergence (break and recovery point), and visual reaction time, and the mean value was used. When both eyes had to be independently measured, the order of the first eye was randomized, and if no statistical significance was found between eyes the mean values were analysed (Armstrong, 2013).

Statistical analysis

All variables tested were subjected to the Shapiro-Wilk test, showing a normal Gaussian distribution. Thus, to analyse the differences on visual function between basketball players and sedentary participants, a separate t-test was performed for independent samples with each variable tested. We used the Bonferroni-correction for multiple comparison. A value of 0.05 was adopted to determine significance.

Results

Sample manipulation check

The t-test for independent samples showed significant differences between basketball players and sedentary participants in the HR (beats/min) ($t_{31} = -7.07, p < 0.001$), RRi (ms) ($t_{31} = 7.09, p < 0.001$), and rMMSD (ms) ($t_{31} = 5.14, p < 0.001$) (**Table 2**). Also, a t-test for independent samples was performed for hours per week of exercise reported by participants ($t_{31} = 21.179, p < 0.001$). Hence, the two samples had different fitness levels.

Visual parameters

Table 3 presents mean values $\pm s$ and significance for all parameters tested in this study.

The analysis for fusional vergence showed that athletes had higher far positive fusional vergence range ($t_{31} = 2.69, p = 0.011$ for the breakpoint, and $t_{31} = 3.02, p = 0.005$ for the recovery value). Regarding near positive fusional vergence, basketball players reached marginally significant higher fusional vergence values for the breakpoint and recovery ($t_{31} = 1.957, p = 0.059$, and $t_{31} = 1.941, p = 0.061$, respectively). For the near point of convergence, closer breakpoints and recovery values were found for athletes ($t_{31} = -3.133, p = 0.004$ and $t_{31} = -2.615, p = 0.014$, respectively).

Finally the accommodative response, facility of accommodation and static near and far stereo acuity yielded no significant differences ($p > 0.05$) between groups (**Table 3**).

Volunteers without basketball background demonstrated significantly higher VDI that did the basketball players ($t_{31} = -3.282$, $p = 0.003$) (Figure 1).

Basketball players showed better scores for eye-hand coordination ($t_{31} = 2.405$, $p = 0.022$). On the other hand, visual-reaction time revealed no differences for liberation and location times ($p = 0.784$ and $p = 0.346$, respectively).

Table 2. Heart rate variability (HRV) at rest, and hours of exercise practice of the 33 participants included in this study by groups.

HRV parameters at rest	Basketball players (n=18)	Sedentary subjects (n=15)	p-value
	M ± s	M ± s	
HR (beats/min)	62.26 ± 7.32	82.86 ± 9.39	< 0.001**
RRi (ms)	992.06 ± 116.73	739.92 ± 84.31	< 0.001**
rMSSD (ms)	694.06 ± 238.28	354.97 ± 149.2	< 0.001**
Exercise practice involvement			
Exercise per week (hours)	10.22 ± 1.73	0.27 ± 0.59	< 0.001**

Note. Asterisk denotes difference with statistical significance between both groups (basketball players and sedentary individuals). ** p values < 0.01.

Table 3. Ocular parameters evaluated according to the measurement method and group analysed. Means and standard deviations were calculated from the mean values of each participant (n=33).

OCULAR MEASUREMENTS		Method		Basketball Players	Sedentary Subjects	p-value
				M ± s	M ± s	
BINOCULAR AND ACCOMMODATIVE FUNCTION	Accommodative response (D)	M.E.M		0.5 ± 0.25	0.375 ± 0.24	0.155
	Accommodative facility (cpm)	Hart chart	cpm	25.67 ± 3.46	27.6 ± 3.36	0.116
			Errors	2.44 ± 2.28	1.27 ± 1.58	0.101
	Near point of convergence (cm)	Push-up	Break point	4.66 ± 1.25	6.24 ± 1.66	0.004**
			Recovery point	7.01 ± 2.68	9.53 ± 2.85	0.014*
	Distance negative fusional vergence (Δ)	Prism bar (steps)	Break value	10.06 ± 4.47	9.6 ± 3.87	0.759
			Recovery value	7.18 ± 2.89	7.47 ± 3.89	0.812
	Distance positive fusional vergence (Δ)	Prism bar (steps)	Break value	26.41 ± 8.03	18.27 ± 9.33	0.011*
			Recovery value	20.06 ± 7.21	12.33 ± 7.44	0.005**
	Near negative fusional vergence (Δ)	Prism bar (steps)	Break value	13.63 ± 3.37	13.07 ± 4.06	0.666
			Recovery value	10.78 ± 3.4	10.67 ± 4.05	0.932
	Near positive fusional vergence (Δ)	Prism bar (steps)	Break value	27.72 ± 8.08	21.2 ± 11.04	0.059
			Recovery value	23.43 ± 7.92	16.93 ± 11.24	0.061
Near static stereo acuity (sec of arc)	Randot Stereotest Circles		38.33 ± 20.72	86.33 ± 128.71	0.128	
Far static stereo acuity (sec of arc)	Stereo D6/D8		84.44 ± 48.17	79.33 ± 72.85	0.811	
VISUAL PERFORMANCE	Visual disturbance index (VDI)	Software Halo v1.0	Binocular	0.41 ± 0.24	0.68 ± 0.23	0.003**
VISUAL-MOTOR PROCESSING	Eye-hand coordination	Wayne Saccadic Fixator	Lights X final speed	2227.61 ± 507.45	1688 ± 774.05	0.022*
	Visual reaction time	Wayne Saccadic Fixator	Liberation	291.89 ± 58.67	286.4 ± 54.49	0.784
			Location	507.39 ± 94.51	463.6 ± 164.73	0.346

Note. Asterisk denotes difference with statistical significance between both groups (basketball players and sedentary subjects). *p values < 0.05, and ** p values < 0.01. M=Mean; s=Standard deviation; M.E.M.=monocular estimated method; Δ=prismatic dioptre; cpm=cycles per minute; cpd=cycles per degree.

Discussion

This investigation incorporates noteworthy findings in several categories: basketball players show a closer near point of convergence for breakpoint and recovery, a larger positive fusional vergence range, a better visual-disturbance index (e.g. lower scores), and higher scores in eye-hand coordination than for sedentary participants.

Accommodative and binocular function

In basketball practice near-far visual changes are persistent for ball interceptions, control, move and trough the ball, analyze the positioning of teammates and opponents, among others (Mangine et al., 2014). These type of actions promote a constant implication of the vergence/accommodative system, which could produce a comparable effect to visual therapy exercises. Exercises based on constant near-far changes in binocular viewing conditions are normally applied in optometry practice with the aim of normalizing the accommodative and vergence system, as well as their mutual interactions (Ciuffreda, 2002). Interestingly, we found that basketball players present a closer near point of convergence and larger far positive fusional vergences in comparison with the sedentary group. Similar results were reported by Christenson & Winkelstein (1988) and Coffey & Reichow (1990), who found a closer near point of convergence and a greater distance vergences range in athletes, respectively. On the contrary, no significant differences were found in the negative fusional vergences between groups in the current study. In agreement, Daum (1982) demonstrated that visual training in young adults with normal binocularity has a significant and prolonged effect on positive vergences, while fusional negative vergences resist change. These substantial differences between the convergence and divergence systems seem to be explained because they are controlled by different neural centers. It is also well known that visual therapy obtains the best results in the treatment of convergence insufficiency, acting on the reduced positive fusional vergences and receded near point of convergence (Scheiman et al., 2005).

No statistical differences were found for near static stereopsis but a tendency to present different values between groups was appreciable (38.33 ± 20.72 for the basketball group versus 86.33 ± 128.71 for the sedentary group). In this line, Boden et al. (2009) found significant differences between baseball/softball players and non-ball player (25.5 ± 11.9 and 56.2 ± 60.7 , respectively). Similarly, we found no differences for far static stereoacuity, and these results are in accordance with Paulus et al. (2014), who compare far static and dynamic stereopsis between professional and amateur soccer players, and individuals without soccer background. The effect of specific eye exercises on stereoacuity seemed to be modest and has a limited use in practical terms (Rawstron, Burley, & Elder, 2005). Therefore, we can expect that systematic basketball practice does not

involve substantial stereopsis improvements. Also, as indicated Paulus et al., (2014) stereopsis tests are not sensitive enough to reveal differences between groups, and further developments in test methodology of stereopsis are required.

The accommodative system is controlled by the autonomic nervous system, and this last is more stable and efficient in athletes (Jafarzadehpur et al., 2007). Therefore, we may expect a better accommodative function in basketball players, but we obtained no significant differences for the accommodative response between groups. We argue two possible explanations, firstly, the possible accommodation variations may be relatively smaller than MEM sensitivity (0.25 D), and more sensitive methods to test accommodative response would be necessary (e.g. open field autorrefractor or wavefront sensors). Secondly and we think most influential, the ball and players are mainly moving at medium-far distances, which does not require a great accommodative demand. So, accommodation enhancements, which require high accommodative stimulation in visual training (Liu et al., 1979), are unlikely to be achieved with only regular basketball practice.

For its part, facility of accommodation in binocular conditions revealed no differences between groups. Scarce comparable work has been conducted, only Jafarzadehpur et al. (2007) found significant differences when they compared professional and intermediate female volleyball players with beginners and non-players, but those differences disappeared when professionals vs intermediates. However, the method of measure used in their work is not clear. Other authors, using a similar methodology to us, showed slightly better accommodative facility for a wide group of interceptive sports athletes than non-athletes (Gao et al., 2015). This investigation not only involves basketball players, but also includes a great variability of sport modalities (tennis, tennis table, baseball, volleyball, badminton), and the visual requirements for each discipline are substantially different.

Visual performance

No study available has investigated visual performance in sports using the visual-disturbance index (VDI). The present study reports a better visual discrimination in athletes (**Figure 5**). It has importance since the perception of halos requires a longer time to recover after exposure to a high-luminance stimulus (e.g. glare) (Dick, Krummenauer, Schwenn, Krist, & Pfeiffer, 1999). The glare phenomenon has great importance in basketball, and players are constantly exposed to glare due to illumination conditions in basketball courts (Sun, Tien, Tsuei, & Pan, 2014). The differences found between basketball players and sedentary individuals could be explained from the perspective that abilities involved during the game are inherently developed while playing the sport (e.g. higher tolerance) (Quevedo-Junyent et al., 2011), as occur with the better selective attention demonstrated in international basketball players (Kioumourtzoglou, Kourteses, Michalopoulou, & Derri, 1998).

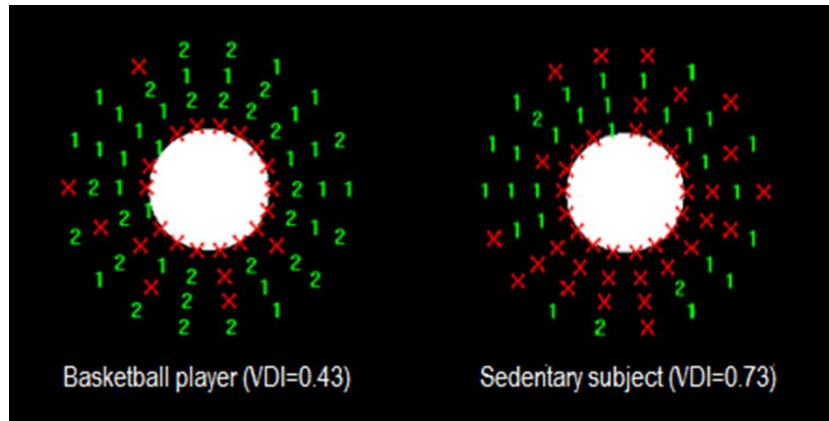


Figure 5. Visual discrimination index (VDI) diagrams of two participants belonging to each experimental group (basketball player number 11, and sedentary participant number 4). Data in green represent correct responses: numbers 1 and 2 indicate if the stimulus was identified just once or both times, respectively. Red crosses indicate that no stimulus was identified in that position.

Visual-information processing

Our results confirm that basketball players show better eye-hand coordination than do individuals without basketball background. This study agrees with Houmourtzoglou et al., (1998) who found a similar result in members of Greek national team, arguing different perceptual strategies from experts to novice in relevant and irrelevant cues. In relation to visual reaction time, previous investigations indicated that players from different disciplines (e.g. water polo or soccer) had faster visual reaction compared with novices or non-athletes, but no differences were found for basketball players, as in this study (Soichi & Oda, 2001). It may demonstrate that the nature of each sport strongly influences on the development of visual skills with constant practice. In the same line, other authors have stated that athletes have a similar speed of response than non-athletes, but there are differences in the ability to detect pertinent cues which is associated with the higher level of expertise in sport (Ripoll, Kerlirzin, Stein, & Reine, 1995).

A plausible explanation

Previous works have supported the contention that differences between athletes and sedentary participants arise from visual-information processing and interpretation rather than from basic visual skills (Del Percio et al., 2007). This study supports the hypothesis that athletes could present a combination of better basic visual function, as well as perceptual and cognitive factors than non-athletes, as explained by several authors (Jafarzadehpur et al., 2007; Quevedo-Junyent et al., 2011; Ryu et al., 2013; Ward & Williams, 2003a). However, this study does not elucidate whether there is an innate visual superiority in athletes or whether those superior skills are achieved due to the constant sport practice. In addition, the different visual demands required in each sport discipline could influence the development of visual, perceptual and cognitive skills. The vast majority of

studies have reported that better visual skills would play a positive role in sports performance. This advantage on visuo-oculomotor abilities can lead to faster and better interceptive skills, motor response, and decision-making (Erickson, 2007; Gao et al., 2015). For example, a recent study indicates that visual tracking speed is related to a greater number of assists and steals, and lower turnovers in NBA players (Mangine et al., 2014). Moreover, considering that our athletes never received specific visual training implies that basketball training in itself might be responsible for the differences in some visual capacities between basketball players and non-players, as explained Alves et al., (2014) for elite soccer players.

Implications for future research

Due to the great amount of sport disciplines, further studies should be performed to analyse the differences for the visual system. We would like to encourage researchers to investigate whether visual training could be transferred to sport performance in field environment. Some work is currently being performed in this area (Schwab & Memmert, 2012), but more data is needed. It would be interesting to explore the possible visual function improvements with systematic sport practice in those persons who present an impaired visual function (e.g. convergence insufficiency, vergence fusional dysfunction).

Conclusions

This article features evidence of the difference between basketball players and sedentary individuals with respect to some skills of their visual function, performance, and processing. Both groups have proved to have different sport backgrounds as reflected by the HRV parameters and as indicated in the demographic questionnaire. In comparison to control group, basketball players clearly present benefits in near point of convergence, positive fusional vergences, halo discriminability, and eye-hand coordination. Our results suggest that systematic basketball practice might be responsible for the development of certain visual abilities.

Study 2. Stronger individuals suffer from higher baseline intraocular pressure

Introduction

Strength training is widely recommended for the general population since it is well known that people with high levels of muscular strength present fewer functional limitations and lower incidences of chronic diseases (Warburton, Nicol, & Bredin, 2006). In a military context, possessing a high level of physical fitness is paramount to carry out ordinary responsibilities (e.g. real and simulated operational missions, war operations) (Tracey & Flower, 2014). This assumption is critical in military fighter aircrew since it is known that higher fitness levels benefit processes involving sustained attention, and reduces physiological responses to mental stress- as flight operations demand (Yen, Hsu, Yang, & Ho, 2009). The importance of a high level of physical fitness increases during combat operations where variable scheduling, circadian disruption or poor sleep quality are frequent (Gore, Webb, & Hermes, 2010). In addition, helicopter pilots are exposed to whole body vibration, which has been associated with back and neck pain. Muscle-strength training reduces the prevalence of pain suffered by helicopter pilots, and they are urged to incorporate exercise into their daily routine (Ang, Monnier, & Harms-Ringdahl, 2009). These responsibilities highlight the need of the soldiers to develop both endurance and strength capabilities. Although the army personnel is encouraged to be involved in physical training programs, they rarely follow structured training plans, and consequently they usually present great disparities in physical fitness. For example, Huerta et al. (2004) found similar fitness levels (measured by VO_{2max}) in a group of Israeli soldiers assigned to field or support units, indicating that differences in exposure to physical activity during military training are insufficient as a means of predicting fitness levels. Similar results were obtained for U.S air Force officers, showing no differences in fitness levels with different military populations (Williford, Sport, Wang, Olson, & Blessing, 1994).

The impact of physical activity has been investigated for a great number of physiological indices such as cardiovascular system (Bertovic et al., 1999; Okamoto, Masuhara, & Ikuta, 2006b; Teixeira et al., 2016), hormonal responses (Sluiter et al., 2000), and electroencephalographic activity (Fontes et al., 2013). As a result of the correlation between ocular functioning and neurocognitive processes (Wilson & O'Donnell, 1988), intraocular pressure (IOP) has been studied due to its sensitivity to physiological factors (Buckingham & Young, 1986). Previous investigations have shown an acute effect of physical activity on IOP. Specifically, IOP tends to decrease immediately after performing moderate aerobic exercise (Najmanova, Pluhacek, &

Botek, 2016; Okuno et al., 2006; Read & Collins, 2011). Recently, Najmanova, Pluhacek & Botek (2016) found that IOP decreased immediately after and 5 and 10 min after 30 min of moderate exercise in a cycloergometer (80 W and 65 RPM), and Okuno et al. (2006) showed that IOP decreases after dynamic exercise (6 min of Master's double two-step test) whereas ocular blood flow increases. On the other hand, high-intensity activities and isometric contractions seem to promote the opposite results (Bakke, Hisdal, & Semb, 2009; Risner et al., 2009; Vieira, Oliveira, de Andrade, Bottaro, & Ritch, 2006). Bakke, Hisdal & Semb (2009) observed an increase in both systemic blood pressure and IOP following a 2-min isometric contraction of the forearm at 40% of participants' maximal voluntary isometric contraction. Vieira et al. (2006) have also reported a significant increase of IOP after performing 4 repetitions with a load equivalent to 80% of the 1-repetition maximum (*IRM*) during the bench press exercise.

It is known that individuals that have high cardiorespiratory fitness have lower IOP compared to those that do not (Risner et al., 2009). Qureshi (1996) showed that increased oxygen uptake after exercise conditioning results in lower baseline IOP, and similarly, Passo et al. (1991) demonstrated that initiation of aerobic exercise training produced a decrease in baseline IOP in healthy participants and glaucoma patients. Therefore, the chronic effect of aerobic activity benefits IOP (lower baseline IOP values) (Natsis et al., 2009; Risner et al., 2009). However, the influence of muscle function (i.e. maximum force, velocity, and power capabilities) on IOP remains underexplored. In this context, the Force-Velocity (F-V) approach to evaluate the maximal capabilities of the muscles to generate force, velocity, and power has gained in popularity over recent years (Jaric, 2015). This approach has been deemed both reliable and valid in different multi-joint exercises such as the squat jump and countermovement jump (Cuk et al., 2014), the supine leg press (Meylan et al., 2015), and the traditional and ballistic bench press exercises (Garcia-Ramos, Jaric, Padial, & Feriche, 2015). Therefore, it seems appropriate to explore the association between the F-V relationship parameters (see Methods section for details) and IOP.

To address the problem discussed above, we determined baseline IOPs as well as the F-V relationship parameters for the ballistic bench press exercise in a group of military combat helicopter pilots. The main objective of the present study was to determine the relationship between the maximal mechanical capabilities of the muscles to generate force, velocity and power and IOP. Based on previous studies that have shown that stronger individuals have higher systemic pulse pressure (Bertovic et al., 1999; Okamoto, Masuhara, & Ikuta, 2006a) and given the relationship between systemic and intraocular pressure (Bakke et al., 2009; Xu, Wang, Wang, & Jonas, 2007), we hypothesized that the participants with higher force capabilities would also have greater baseline IOP values.

Methods

Ethical approval

We conducted the study in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki). The experiment was carried out under the guidelines of the University of Granada's Institutional Review Board (IRB approval 112/CEIH/2016) and written informed consent was obtained from each pilot prior to the study. All participants were informed about their right to leave the experiment at any time.

Participants

23 male volunteer military combat helicopter pilots belonging to the Spanish Army Airmobile Force (FAMET) at the airbase of Almagro (Ciudad Real, Spain) (mean age \pm SD: 37.22 \pm 8.05) took part in the experiment. All volunteers were members of the Attack Helicopter Battalion BHELA I. Fifteen of them were qualified to fly the EC665 Tigre attack helicopter, constituting the entire team of Spanish Tigre pilots, and eight out of the twenty-three flew the Messerschmitt-Bölkow-Blohm Bo 105 helicopter. All volunteers were on flight status, had a recent verification of good health and were free of medication. They had normal or corrected to normal vision. On the day of testing, all pilots were instructed to avoid alcohol consumption, caffeine beverages and vigorous exercise, and were also asked to sleep adequately the night prior to testing.

Instruments and Measurements

Body composition assessments

A dual-energy X-ray absorptiometry (DXA) (Hologic Explorer scanner, Hologic Corp., Bedford, MA, USA) was used for assessing body composition, which is considered a gold standard (Castro-Piñero et al., 2009). The DXA was calibrated using a lumbar spine phantom as recommended by the manufacturer. For the whole body measurements, pilots were scanned in the supine position with the highest resolution. Analysis were performed using the extended research mode according to the operating manual. Bone mineral density (g/cm^2), lean mass (kg), and fat mass (kg) are displayed in **Table 4**.

Table 4. Participant's Demographics.

Sample characteristics	Military helicopter pilots (n=23)
	M (SD), range
Age (years)	37.22 (8.05), 25 - 52
Height (cm)	177.61 (5.55), 170 - 185.5
Weight (Kg)	80.51 (9.26), 66 – 101.2
Body mass index (kg/m ²)	25.48 (2.49), 21.9-33
Bone mineral density (g/cm ²)	1263.65 (88.58), 1117 - 1470
Lean mass (kg)	57.71 (5.41), 48.25 – 70.42
Fat mass (kg)	18.5 (4.72), 10.18 – 26.36

Abbreviations: M, Mean; SD, Standard deviation

Ballistic bench press

The warm-up included dynamic stretching, arm and shoulder mobilization, and 1 set of 4 repetitions with an external load of 17 kg (mass of the Smith machine bar) during the ballistic bench press exercise. Thereafter, an incremental loading test was performed. Initial load was set at 20 kg for all participants, and was progressively increased in 2.5, 5, or 10 kg increments until the attained peak velocity was lower than 1.5 m·s⁻¹ [\approx 50% of *1-RM* according to García-Ramos et al. (2015)]. The bench press procedure followed a standard "touch-and-go" protocol in which the bar was lowered slowly to touch the chest before being lifted immediately at the maximum possible speed.

The load corresponding to a peak velocity equal to 1.5 m·s⁻¹ was doubled to determine the bench press *1-RM*. If the participants were able to lift this load at a mean velocity \leq 0.25 m·s⁻¹ it was considered their real *1-RM*. The load was reduced (if pilots were not able to complete the repetition) or incremented (if volunteers lifted the load faster than 0.25 m·s⁻¹) from 1 to 5 kg until determining their real *1-RM*. Participants needed an average of 1.8 \pm 0.7 attempts to achieve their *1-RM*.

The participants performed 2 repetitions at the maximum possible speed with each load, but only the repetition with the highest mean propulsive velocity was used for subsequent analysis. The rest period between trials with the same load was 1 min and 4–5 min between different loads conditions. Two trained spotters were present on each side of the bar during the protocols to ensure safety, as well as to verbally encourage the participants throughout the test.

All trials were performed in a Smith machine (Technogym, Barcelona, Spain). A dynamic measurement system (T-Force System; Ergotech, Murcia, Spain) validated by Sánchez-Medina & González-Badillo (2011) was fixed perpendicularly to the bar with a tether and reported its

vertical instantaneous velocity with a sampled rate of 1,000 Hz. This device consists of a linear velocity transducer interfaced to a personal computer using a 14-bit resolution analog-to-digital data acquisition board and custom software. A complete description of this device is provided elsewhere (Sánchez-Medina & González-Badillo, 2011).

Mean values of force and velocity within the propulsive phase (i.e., time interval from the start of the concentric phase until the bar acceleration is $< -9.81 \text{ m}\cdot\text{s}^{-2}$) were obtained. The averaged force-velocity relationships were assessed from individual force and velocity data obtained under a minimum of 4 loading magnitudes according to Sreckovic et al. (2015) [$F(V) = F_0 - aV$], where F_0 represents the Force-intercept (i.e., force at zero velocity), a is the slope that corresponds to F_0/V_0 , and V_0 is the Velocity-intercept (i.e., velocity at zero force). The linear regressions directly revealed the maximum force (F_0) and slopes (a). Maximum velocity (V_0) and maximum power (P_0) were calculated as $V_0 = F_0/a$, and $P_0 = (F_0 \cdot V_0)/4$, respectively. The averaged values of force used to calculate the F–V relationship parameters (F_0 , V_0 , a , and P_0) as well as the 1RM value were also normalized per kg of body mass. The typical force-velocity profile of a representative participant is illustrated in **Figure 6**.

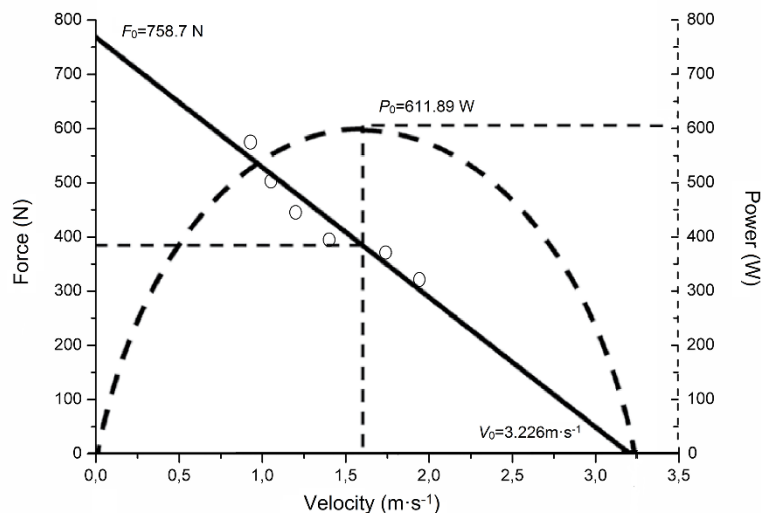


Figure 6. Force-Velocity relationship of a representative participant of the study sample. F_0 , theoretical maximal force; V_0 , theoretical maximal velocity; P_0 , theoretical maximal power. P_0 was calculated as $(F_0 \cdot V_0)/4$.

Intraocular pressure

IOP measures were obtained by rebound tonometry using an Icare Tonometer (Tiolat Oy, INC. Helsinki, Finland) and before any physical effort (baseline measure). This apparatus has been demonstrated to be in accordance with the Goldmann applanation tonometry (GAT), which is widely accepted as the gold standard for IOP measurements (Davies, Bartlett, Mallen, &

Wolffsohn, 2006). However, the Icare tonometer has the advantage that it is easy to use, records IOP measurements in situ without the need for topical anesthesia and slit lamp, and is more comfortable than GAT. Therefore, using this hand-held portable tonometer is recommended in practical terms. We followed the recommendations given by Armstrong (2013) for analysis of data obtained from both eyes. This study indicates that when the correlation between eyes is close to 1, then data from both eyes could be averaged.

The order in which the first eye was measured was randomized (Armstrong, 2013). Participants were instructed to look at distance while the probe of the tonometer was held at a distance of 4 to 8 mm, and perpendicular to cornea. Six rapid consecutive measurements were performed against the central cornea and the mean reading was displayed digitally in mmHg on the LCD screen. The apparatus indicates if differences between measures are acceptable or if the standard deviation (SD) is too large and a new measurement is recommended; we always obtained values with low SD (ideal measure). Participants were asked to remain seated for 5 minutes in a quiet room before IOP measures. To enhance internal validity, IOP measurements were taken twice, with a 3 min interval between them. Thus, we calculated the average IOP from 4 IOP measurements (2 readings for each eye).

Procedure

The experimental protocol consisted of a single session with three different phases. After signing the consent form, in the first phase, participants were scanned in the DXA for body composition assessment. During the second phase, we instructed participants to remain seated for 5 minutes, and an experienced optometrist took IOP measures. Finally, in the third phase, participants performed the ballistic bench press test. The baseline IOP and the strength test were measured under the same illumination conditions (~ 250 lux), at a comfortable temperature, and isolated from external noise.

Statistical Analysis

To check normality of data, all variables tested were subjected to the Shapiro-Wilk test, showing a normal Gaussian distribution ($P > .05$). An α of .05 was adopted to determine significance.

Linear regression analyses were carried out to ensure F-V relationships throughout participants.

Baseline IOP was calculated as the mean value from both eyes (Armstrong, 2013), and the mean value was also calculated from the two measurements taken. Thus, we performed intraclass correlational analysis between eyes (right eye vs left eye). Consequently, we also obtained intraclass correlation coefficients for the measurement moment (first and second measure).

Bivariate correlations were performed for absolute and normalized parameters derived from the individual F–V relationship (F_0 , V_0 , P_0) and 1-RM , body composition (bone mineral density, fat mass, and lean mass), and baseline IOP.

Results

Strength Parameters

The descriptive values of the F–V relationship parameters as well as the 1-RM strength are shown in **Table 5**. The individual F–V relationships proved to be remarkably strong and fairly linear with Pearson’s product-moment correlation coefficient of 0.982 (0.785–1.000). The 1-RM was strongly correlated with F_0 ($r = 0.862$, $P < .001$).

Strength parameters	Absolute values	Normalized values
	M ± SD	M ± SD
F_0	675.19 ± 123.87 N	8.41 ± 1.26 N·kg ⁻¹
V_0	3.59 ± 0.5 m·s ⁻¹	
P_0	604.68 ± 134.39 W	7.53 ± 1.44 W·kg ⁻¹
1-RM	75.02 ± 14.44 kg	0.94 ± 0.16 kg·kg ⁻¹

Table 5. Absolute and normalized values of the force-velocity relationship parameters and the 1 repetition maximum.

Abbreviation: M, mean; SD, Standard deviation; F_0 , theoretical maximal force; V_0 , theoretical maximal velocity; P_0 , theoretical maximal power; 1-RM , 1-repetition maximum.

Baseline IOP

Statistical guidelines to analyze data from both eyes indicate that investigators have to ensure that there are no differences between eyes, and in that case the average value can be used for further analysis (Armstrong, 2013). Intraclass correlation coefficient between eyes was close to 1 (0.964), and therefore we considered the mean intraocular pressure value between eyes for further analysis. Similarly, we performed the same analysis to test the differences between both IOP readings taken in different moments (3 min break interval), and we obtained an intraclass correlation coefficient of 0.985. Therefore, because no differences were found, the mean value (mean value ± SD: 14.54 ± 2.85) from both measurements was the one used in this study.

Correlational Analysis

We performed a Pearson bivariate correlation to test the predictive validity of baseline IOP with strength parameters (absolute and normalized) and body composition indices. Baseline IOP showed a significant positive correlation with several strength parameters: maximum force (F_0) ($r_{23} = .418$, $P = .047$), maximum power (P_0) ($r_{23} = 0.557$, $P = .006$, see **Figure 7**), maximum

dynamic strength (*I-RM*) ($r_{23}=0.430$, $P = .040$), and relative maximum power ($r_{23}=0.471$, $P = .023$); a marginal significance was found for absolute maximum velocity ($r_{23}=0.378$, $P = .075$). No significance for any index was found in regard to body composition parameters ($P > .05$). All correlations are displayed in **Table 6**.

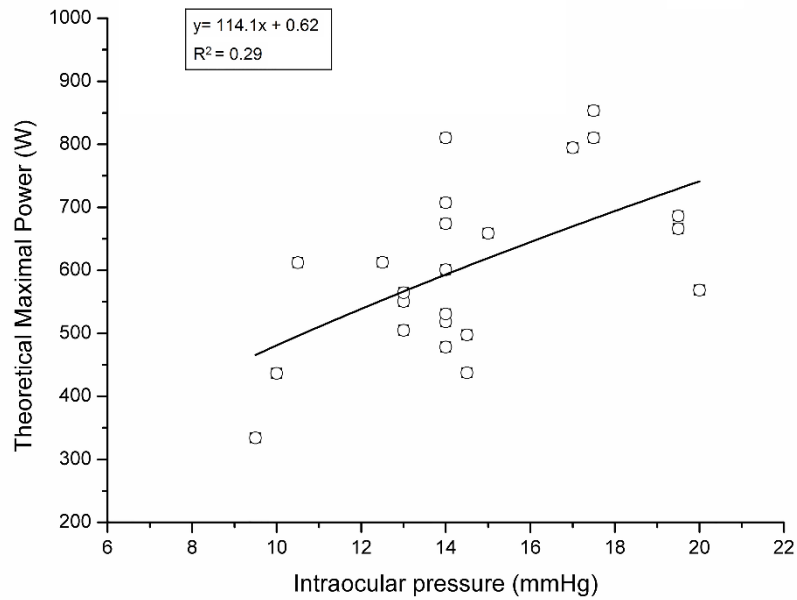


Figure 7. Linear regression analysis showing the correlation between the baseline intraocular pressure (IOP) and the theoretical maximal power (P_0). Open circles represent data for the entire sample ($n=23$). ($P < .01$, $r_{23} = 0.557$).

Table 6. Bivariate correlations between baseline IOP, strength parameters (absolute and normalized), and body composition indices.

	BMI	BMD	LM	FM	F_0	V_0	P_0	$1-RM$	F_{0r}	P_{0r}	$1-RMr$
	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)	r (p-value)
IOP	0.256(0.238)	0.52 (0.814)	0.329 (0.125)	0.138 (0.531)	0.418 (0.047) ^a	0.378 (0.75)	0.557 (0.006) ^b	0.430 (0.04) ^a	0.276 (0.202)	0.471 (0.023) ^a	0.268 (0.216)
BMI		0.393 (0.064)	0.728 (<0.001) ^b	0.72 (<0.001) ^b	0.569 (0.005) ^b	0.013 (0.953)	0.498 (0.016) ^a	0.03 (0.891)	0.030 (0.891)	0.049 (0.825)	-0.044(0.843)
BMD			0.406 (0.054)	-0.029 (0.895)	0.548 (0.007) ^b	-0.014 (0.950)	0.464 (0.026) ^a	0.528 (0.01) ^b	0.428 (0.042) ^a	0.353 (0.098)	0.372 (0.081)
LM				0.504 (0.014)*	0.779 (<0.001) ^b	0.148 (0.499)	0.741 (<0.001) ^b	0.732 (<0.001) ^b	0.248 (0.253)	0.309 (0.152)	0.202 (0.355)
FM					0.143 (0.514)	-0.054 (0.806)	0.086 (0.696)	0.016 (0.941)	-0.485 (0.019) ^a	-0.417 (0.048) ^a	-0.559 (0.006) ^b
F_0						-0.029 (0.896)	0.803 (<0.001) ^b	0.862 (<0.001) ^b	0.76 (<0.001) ^b	0.567 (0.005) ^b	0.553 (0.006) ^b
V_0							0.561 (0.005) ^b	0.382 (0.72)	-0.07 (0.75)	0.633 (0.001) ^b	0.394 (0.063)
P_0								0.935 (<0.001) ^b	0.578 (0.004) ^b	0.844(<0.001) ^b	0.683(<0.001) ^b
RM									0.686 (<0.001) ^b	0.794 (<0.001) ^b	0.788(<0.001) ^b
F_{0r}										0.72 (<0.001) ^b	0.821 (<0.001) ^b
P_{0r}											0.901 (<0.001) ^b

Abbreviations: IOP, Intraocular pressure; BMI, Body Mass Index; BMD, Bone Mineral Density; LM, lean mass; FM, fat mass; F_0 , theoretical maximum force; V_0 , theoretical maximum velocity; P_0 , theoretical maximum power; $1-RM$, repetition maximum; F_{0r} , relative theoretical maximum force; P_{0r} , relative theoretical maximum power; $1-RMr$, relative repetition maximum; r, Pearson correlations coefficients.

^a Significant differences ($P < .05$)

^b Significant differences ($P < .01$)

Discussion

Results show that, as hypothesized, IOP correlates positively with some F-V relationship parameters (F_0 and P_0) obtained from the ballistic bench press, as well as with the bench press maximum dynamic strength ($1-RM$). These findings could indicate that stronger individuals present higher baseline intraocular pressure values. Previous studies have reported the acute effect in IOP of aerobic (Najmanova et al., 2016; Read & Collins, 2011) and anaerobic (Bakke et al., 2009; Rüfer et al., 2014; Vieira et al., 2006) physical activity, and also how involvement in aerobic physical training decreases IOP (Risner et al., 2009). However, to the best of our knowledge, this is the first investigation that has explored the relationship between the F-V parameters (upper-body) and baseline IOP.

The F-V relationship is used to evaluate the maximal mechanical capabilities of the neuromuscular system to produce force, velocity and power. This approach is based on the assumption that the F-V relationship during multi-joint maximum performance tasks is strong and fairly linear (Jaric, 2015), an assumption that has been supported by our results ($r_{23} = 0.982$). In addition, the parameters obtained from the F-V relationship have proved to provide high reliability, validity, and sensitivity (Garcia-Ramos et al., 2015). The significant correlations found in the current study between the 1RM and F_0 ($r_{23} = 0.862$, $P < .001$) further support the validity of the F_0 parameter to evaluate maximal force capabilities.

The association between anthropometrical characteristics (e.g. BMI, adiposity markers) and IOP is controversial in the related literature. A previous study demonstrated a positive correlation between BMI and IOP (Cheung & Wong, 2007), although others authors found no significant association for those indices (Chan et al., 2016). Chan et al. (2016) indicated that systolic blood pressure often masked the relationship between IOP and BMI in a large-scale multisite cohort study. Higher levels of obesity and particularly central obesity (waist circumference) was associated with higher IOP values (Zhao et al., 2016). Likewise, Janssen, Katzmarzyk & Ross (2004) indicated that waist circumference and not BMI presented an obesity-related health risk. These views are beyond the scope of our study and also need larger samples to achieve solid results, but the advance body composition analysis (dual-energy X-ray absorptiometry) performed by our sample yielded no significant association between baseline IOP and anthropometrical characteristics such as BMI, fat mass, lean mass or bone mineral density ($p > 0.05$). Clearly, further research is needed to understand this possible association, including exhaustive body composition assessments and controlling cardiovascular factors (e.g. diastolic blood pressure, systolic blood and pulse rate) before performing correlational analyses with intraocular pressure.

Understanding the consequences that affect intraocular pressure is crucial to determining the best physical training and which type of exercises are recommended for glaucoma patients or potential sufferers. It is also important to consider the possible long term consequences in ocular health of strength activities in a healthy population, and especially in those at risk of glaucomatous pathology (Williams, 2009). Different conditions have been associated with increasing IOP, Mori et al. (2000) found a positive correlation between hypertension and IOP. A positive correlation between systolic and diastolic blood pressures and IOP has been demonstrated (Klein, Klein, & Knudtson, 2005; Mitchell, Lee, Wang, & Rochtchina, 2005; Xu et al., 2007). According to the effect of diastolic blood pressure on IOP, this relationship has been explained as a consequence of increased ultrafiltration of the aqueous humour due to the higher ciliary artery pressure (Lee et al., 2002). Parallel to those investigations, resistance training has been demonstrated to decrease arterial distensibility, and only regular moderate physical activity preserves endothelial function (Di Francescomarino, Sciartilli, Di Valerio, Di Baldassarre, & Gallina, 2009). Several studies have found that strength training is associated with reduced central arterial compliance in young men, which is associated with an increased risk for coronary heart disease (Alan et al., 2003; Miyachi et al., 2004). Bertovic et al. (1999) found that muscular strength training is associated with low arterial compliance and high pulse pressure. Our results and the previous literature suggest that any condition, higher muscular strength in this study, which promotes cardiovascular alteration (e.g. higher blood pressure) could exacerbate intraocular pressure values. Furthermore, our study indicates that higher strength levels are moderately associated with higher baseline IOP.

Implications for future research and current limitations

The possibility that exercise could be a useful tool in eye health has been speculated (Risner et al., 2009). Careful IOP management has to be undertaken in glaucoma sufferers since IOP reduction is beneficial for control of this disease (Zhao et al., 2016). Therefore, the performance of strength training could have profound consequences in glaucoma management and should be considered in exercise prescription (Rüfer et al., 2014). Clearly, further studies should consider different strength training programs which produce a broad range of corporal adaptation processes (e.g. cardiovascular system) and include the effect on IOP as the dependent variable. It would be of interest to examine whether people who regularly perform anaerobic exercise (e.g. military personnel, weightlifters, etc.) were at greater risk of developing glaucoma. The higher IOP to which strength exercisers expose their eyes could have negative consequences and promote a progressive optic neuropathy by retinal ganglion cell death. Recent advances in IOP continuous monitoring technology employing a contact lens sensor (Sensimed Triggerfish, Lausanne, Switzerland) have been proven beneficial for glaucoma management (Mansouri, Weinreb, & Liu, 2015). In the future these wearable devices may allow the evaluation of IOP changes induced by exercise. In terms of limitations, this study has only analyzed upper-body strength parameters in

male participants. Hence, the authors recommend further investigation to scrutinise our novel results with larger samples, including lower body strengthening protocols and female participants. In spite of the wide age range and fitness level of our sample, next investigations should consider age and fitness level in their experimental designs.

Conclusions

This article features evidence of the moderate positive correlation between strength indices and IOP. Stronger participants in ballistic bench press show higher baseline IOP values. We consider that corporal adaptation processes modify IOP, as occurs with another cardiovascular biomarkers. Two important applications should be considered as a result of this investigation: (1) Strength training could have negative consequences in terms of achieving low IOP values, which especially important in glaucoma patients (2) repeated exposure to strength exercise, which produces an increased IOP, could contribute to new or additional glaucomatous pathological change in susceptible individuals. Further research is required in this regard.

Study 3. The performance of strength exercises induces an instantaneous rise in intraocular pressure

Introduction

The autonomic innervation plays a crucial role in regulating the intraocular pressure (IOP) levels (Neuhuber & Schrödl, 2011). Different circumstances (e.g. circadian variations, physical activity, cognitive processing, and lifestyle) can alter the autonomic nervous system, and therefore, the level of IOP (Agnifili et al., 2015; Risner et al., 2009; Vera et al., 2016). Due to the fact that IOP fluctuations are strongly implicated in the development of glaucoma, the key factor to prevent ocular damages is IOP reduction and stabilization (Zhao et al., 2016). Moreover, the estimation of IOP behaviour as a consequence of autonomic variations must be taken into account in order to preserve ocular health.

Strength training has proven to be effective in improving individuals' health status (Westcott, 2012). For example, Warburton, Nicol, & Bredin (2006) concluded that intervention programs designed specifically to enhance muscular strength, muscular endurance, muscular power, and flexibility helped to improve several indicators of health status. For this reason, these type of training programs are recommended to be performed at least twice a week in order to maintain functional status and enhance quality of life (Blair, LaMonte, & Nichaman, 2004). However, special care should be taken when strength training is undertaken by populations with certain cardiovascular pathologies or risk factors as there may be undesirable side-effects (Miyachi et al., 2004).

Recent studies have focused on the acute effect of strength training on IOP, which could have relevance on IOP management for glaucoma patients or potential sufferers. In this regard, Vieira, Oliveira, de Andrade, Bottaro, & Ritch, (2006) investigated the effect of 4 repetitions at 80%RM in the bench press exercise with and without holding the breath, finding significant IOP increases following the bench press protocol, and even greater when participants held their breath. Similarly, Rüfer et al., (2014) found that upper limb physical anaerobic effort (20 repetitions with 65%RM on the butterfly machine) induced a significant IOP rise, whereas a leg curl exercise did not promote any significant change on IOP after performing 20 and 10 repetitions at 65%RM and 75%RM, respectively. Although further research is required, it seems that the part of the body mainly involved and the exercise intensity have relevance in IOP changes during strength training. The five basic resistance training exercises are the squat, deadlift, bench press, pull-ups, and military press. Surprisingly, although these exercises are key in any resistance training

programme, there is no information regarding the effect of the intensity (%RM) of lifting in these exercise on IOP behaviour.

To address the problem discussed above, we determined baseline IOPs as well as the IOP after 4-5 progressive loads in the bench press and jump squat exercises. The aims of the present study were to (1) examine the effect of the intensity (%RM) of the exercise on IOP, and (2) compare IOP values between the ballistic bench press and jump squat exercises for the same relative loads. We hypothesized that (1) IOP could linearly increase with load as a consequence of higher muscular requirements and longer time under muscular tension, and also that (2) the bench press would elicit higher IOP values than the jump squat for the same relative load due to the fact that this exercise is performed in supine position (McMonnies, 2016).

Methods

Participants

We conducted the study in conformity with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and permission was provided by the university Institutional Review Board (IRB approval 112/CEIH/2016). 20 male military officers belonging to the Spanish Army Training and Doctrine Command (Granada, Spain) were enrolled in this study. All participants had a recent verification of good health and successfully underwent the annual physical tests of the Spanish Army, and all of them were free of medication. They had normal or corrected to normal vision, and had no history of ocular disease or surgery. We imposed as inclusion criteria 1) baseline IOP readings below to 21 mmHg, and 2) all candidates were able to attain a peak velocity $\geq 1.5 \text{ m}\cdot\text{s}^{-1}$ for all the incremental loads with the exception of bench press 1-RM. Additionally, on the day of testing, all pilots were instructed to avoid alcohol consumption, and perform any exercise. Also, they were asked to sleep adequately the night prior to testing. We excluded two participants because they declined to participate in the squat test due to previous injuries, and other participant did not finish the entire protocol because he was not able to move the bar at the peak velocity determined. As a result, we analysed data from 17 out of 20 participants ($M \pm SD$: 46 ± 4.77 years).

Materials and measurements

Jump squat

The warm-up included jogging, joint mobility, dynamic stretching, six countermovement jumps without additional weight, and one set of five jumps lifting 17 kg in the assessed exercise. Participants then performed an incremental loading test at four different intensities of the

countermovement jump exercise performed in a Smith machine. The loads used were 20, 40, 60, and 80% of body weight. Participants performed two repetitions as quickly as possible with each load and rested for one min between trials with the same load and five min between different loads. Two trained spotters were present on each side of the bar during the protocols to ensure safety, as well as to verbally encourage the participants throughout the test.

Ballistic bench press

The warm-up included dynamic stretching, arm and shoulder mobilization, and one set of four repetitions during the Smith machine bench press throw with an external load of 17 kg. Thereafter, an incremental loading test at four different intensities of the ballistic bench press exercise was performed in a Smith machine. Initial load was set at 20 kg for all participants. This load was progressively increased in 2.5, 5, or 10 kg based on the maximum velocity of the bar recorded by a linear velocity transducer (T-Force System; Ergotech, Murcia, Spain). The increase of the load was proportional to the recorded velocity of the bar in such a way that the last load of the protocol was always performed at a maximum velocity of $\approx 1.4 \text{ m}\cdot\text{s}^{-1}$. Participants performed two repetitions with each load using the standard "touch-and-go" protocol in which the bar was lowered slowly to touch the chest before being lifted immediately at the maximum possible speed. The rest period between trials with the same load was one min and between different loads was five min. Two trained spotters were present on each side of the bar during the protocols to ensure safety, as well as to verbally encourage the participants throughout the test.

The load corresponding to a maximum velocity equal to $1.5 \text{ m}\cdot\text{s}^{-1}$ ($\approx 50\%$ of 1RM according to García-Ramos et al., 2015) was doubled to determine the bench press 1RM. If the participants were able to lift this load at a mean velocity $\leq 0.25 \text{ m}\cdot\text{s}^{-1}$ it was considered their real 1RM. The load was reduced (if subjects were not able to complete the repetition) or incremented (if subjects lifted the load faster than $0.25 \text{ m}\cdot\text{s}^{-1}$) from 1 to 5 kg until determining their real 1RM. Participants needed an average of 1.9 ± 0.6 attempts to achieve their 1RM.

Intraocular pressure

We measured IOP with a portable rebound tonometer (ICare, Tiolat Oy, INC. Helsinki, Finland) in a randomly selected eye, using the same eye for all subsequent IOP measures. This apparatus has shown good intra- and interobserver reproducibility, and it has been utilised in similar investigations (Rüfer et al., 2014). Participants were instructed to look at distance while the probe of the tonometer was held at a distance of 4 to 8 mm, and perpendicular to cornea. Six rapid consecutive measurements were performed against the central cornea and the mean reading was displayed digitally in mmHg on the LCD screen. The apparatus indicates if differences between

measures are acceptable or if the standard deviation (SD) is too large and a new measurement is recommended; we always obtained values with low SD (ideal measure).

Procedure

Firstly, participants signed the consent form and filled in the demographic questionnaire. Thereafter, we took the IOP baseline measure and participants were instructed to warm-up. At this point, we explained to the participants how to correctly execute the two exercises and they began with the corresponding test. Right after the second repetition of each incremental load, we measured IOP in a standing position with the exception of bench press 1-RM where just one repetition was carried out with the corresponding load. After the first incremental test, participants were asked to rest for 10 min, and then we followed the same protocol for the second test (counterbalanced order). Finally, to avoid diurnal fluctuation that can affect physical performance (Reilly et al., 2007) and IOP measures (Agnifili et al., 2015), all experimental sessions were conducted between 10 am and noon (12pm).

Experimental design and statistical analysis

A repeated-measures design was used to examine the effect of an incremental loading test in the bench press and jump squat exercises on intraocular pressure. A one-way repeated measures ANOVA was separately applied for the jump squat (5 measurements: baseline, and loads 1, 2, 3, and 4) and bench press (6 measurements: baseline, loads 1, 2, 3, and 4, and 1RM) to examine the effect of the load on IOP. Additionally, the effect of the type of exercise on IOP was assessed through a two-way repeated measures ANOVA (exercise [Squat vs Bench press] × intensity [50%RM vs 60%RM]). When significant F values were achieved, pairwise differences between means were identified using Bonferroni post hoc procedures.

Results

Jump Squat

The 4 consecutive absolute loads used during the test were 96.44 ± 8.33 kg (50.75 ± 4.69 %RM), 110.96 ± 11.52 kg (58.33 ± 5.66 %RM), 126.29 ± 12.55 kg (66.38 ± 6.17 %RM), and 139.26 ± 12.94 kg (73.19 ± 6.1 %RM). The one-way ANOVA conducted on IOP values during the jump squat incremental loading test to be significant, $F(4,64) = 16.18$, $p < .001$, $\eta_p^2 = 1$, (see **Table 7**, and **Figure 8** [panel A]). The increase in the load was strongly associated with a linear increase in IOP ($r = .936$; **Figure 8** [panel B]). Bonferroni post hoc procedures revealed that the highest

intensity (~ 75 %RM) was the only one able to promote significant differences in IOP with respect to the baseline measure and the other three loads ($p < .001$, $p < .001$, $p < .001$, and $p = .009$, respectively).

Table 7. Average and standard deviation of IOP values at different intensities for the jump squat and the bench press exercise.

Jump squat: M (SD)					
IOP (mmHg)	baseline	50%RM	60%RM	65%RM	75%RM
	14.29 (2.47)	14.18 (3.11)	15.18 (2.7)	15.94 (2.25)	17.94 (2.84)

Bench press: M (SD)						
IOP (mmHg)	baseline	30%RM	40%RM	50%RM	60%RM	1-RM
	14.24 (2.66)	14.76 (3.01)	15.47 (2.32)	16.76 (1.95)	18.18 (1.85)	19.82 (2.9)

Note. M=Mean, SD=Standard Deviation, IOP=Intraocular pressure, RM=repetition maximum.

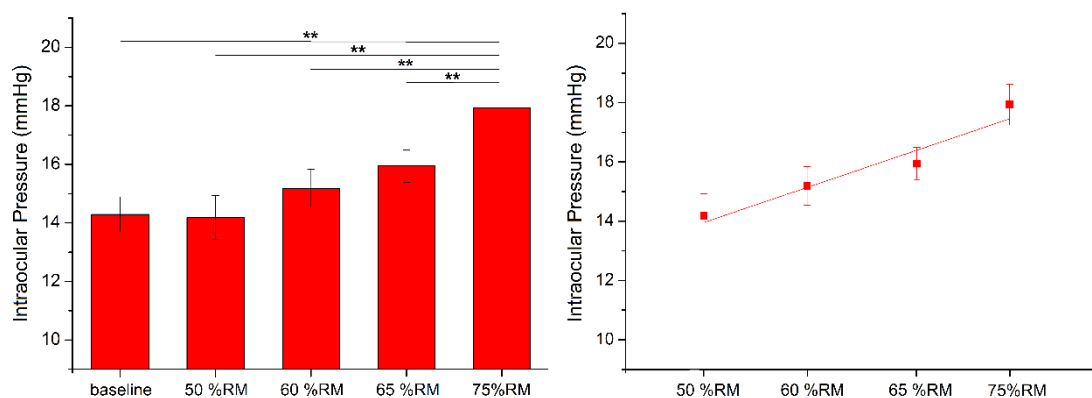


Figure 8. A) Effects of performing jump squats at different intensities on IOP. B) Linear regression analysis showing the correlation between intraocular pressure and the four absolute loads used. In the panel A) the mean intraocular pressure in the baseline reading and just after exercise in the four consecutive loads are displayed. Panel B) illustrates the linear association of intraocular pressure with the four loads implemented ($y = 6.05x + 0.16$; $r^2 = 0.88$). The x-axis shows the moment of measurement, considering the baseline assessment (panel A) and the relative loads. ** indicates statistically significant differences between the measurement (corrected p-value < 0.01). Errors bars represent the Standard Error (SE). All values are calculated across participants ($n=17$).

Bench press

For the bench press test, the external loads used were 19.53 ± 1.94 kg (30.88 ± 4.61 %RM), 26.65 ± 3.33 kg (41.8 ± 3.97 %RM), 32.41 ± 4.89 kg (50.65 ± 4.46 %RM), 37.53 ± 5.6 kg (58.67 ± 5.25 %RM), and 64.35 ± 10.65 kg (1RM). The one-way ANOVA with the within-participants factor of load revealed statistical significance for mean IOP values when executing the bench press incremental loading test, $F(5, 80) = 42.627$, $p < .001$, $\eta_p^2 = 1$, (see **Table 7**, and **Figure 9** [panel A]). Similar to the jump squat test, we found that IOP linearly increases with external loads ($r = .968$; **Figure 9** [panel B]). The multiple comparison analysis showed that ~ 50 RM% was enough to produce significant changes in IOP in comparison with the baseline IOP value ($p = .001$ for ~ 50 RM%, $p < .001$ for ~ 60 RM%, and $p < .001$ for the 1RM).

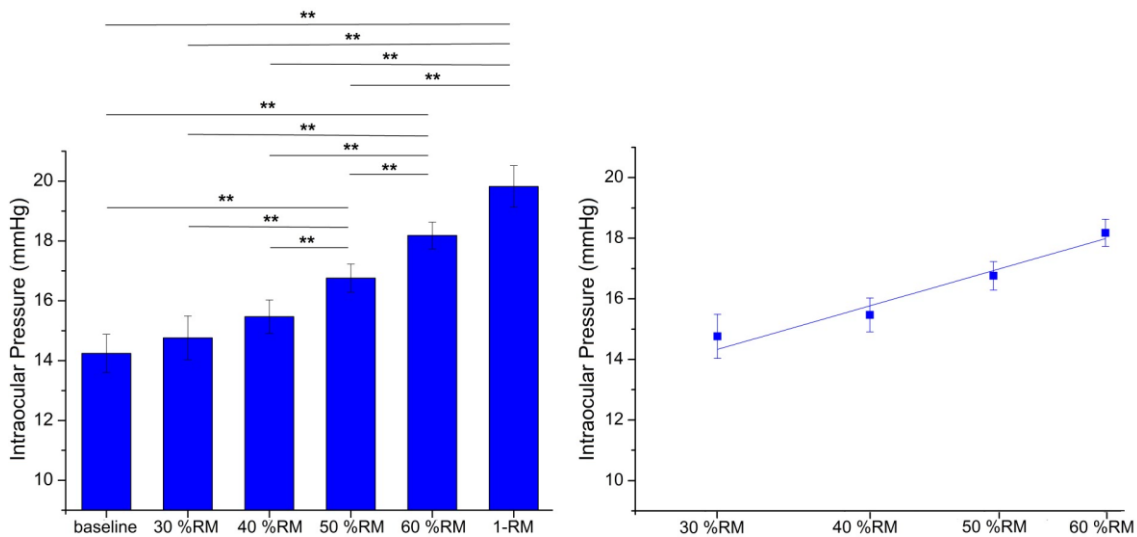


Figure 9. A) Effects of performing ballistic bench press at different intensities. B) Linear regression analysis showing the correlation between intraocular pressure and the four absolute loads used. In the panel A) the mean intraocular pressure in the baseline reading and just after exercise in the four consecutive loads and the one maximum repetition are displayed. Panel B) represents the linear association of intraocular pressure increase with the four loads implemented ($y = 10.26x + 0.13$; $r^2 = 0.94$). The x-axis shows the moment of measurement, considering the baseline assessment (panel A) and the relative loads. ** indicates statistically significant differences between the measurement moments (corrected p-value < 0.01). Errors bars represent the Standard Error (SE). All values are calculated across participants ($n = 17$).

Jump squat vs Bench press

The two-way repeated measures ANOVA revealed significant main effects for exercise ($F(1,16) = 20.315$, $p < .001$, $\eta_p^2 = .988$), and intensity ($F(1,16) = 37.564$, $p < .001$, $\eta_p^2 = 1$), but the interaction did not show statistical differences ($F < 1$). IOP values were significantly higher for the bench press than the jump squat for the same relative intensities (**Figure 10**).

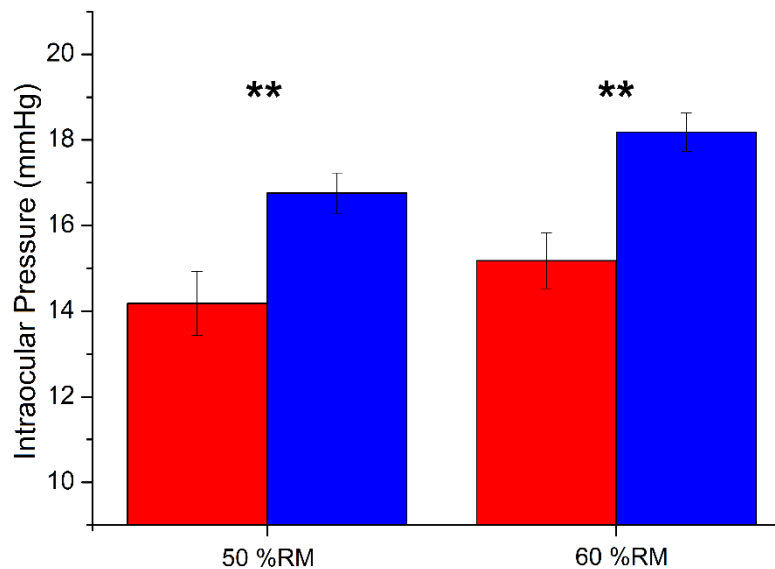


Figure 10. The effect of the type of exercise on IOP at the same relative intensities. Average intraocular pressure values for each exercise (squat vs bench press) at 50 and 60 %RM. Data from the squat exercise are represented in red and from the ballistic bench press in blue. ** indicates statistically significant differences between the two exercises (corrected p-value < 0.01). Errors bars represent the Standard Error (SE). All values are calculated across participants ($n=17$).

Discussion

IOP is sensitive to homeostatic disturbances caused by physical tasks among other types of activities. However the effect of exercise, mainly anaerobic, on IOP is not firmly established. We tested two of the main basic and popular resistance training exercises (jump squat and bench press) with several progressive loads. Our results show that, as hypothesized, the acute performance of strength training exercises increases IOP. The magnitudes of the changes in IOP are dependent on both the intensity and the exercise type. The increase in the load is associated with an increase in IOP, and for the same relative load (%RM) the increase in IOP is higher during the bench press throw than during the jump squat. These findings support the idea that physical efforts which interfere the regular interchange of respiratory gases (e.g. Valsalva manoeuvre, which occur with a closed glottis) and promote homeostatic variations cause an IOP rise.

The performance of low-intensity exercise has been associated with a decrease or unchanged IOP (Najmanova et al., 2016; Natsis et al., 2009; Read & Collins, 2011; Risner et al., 2009; Roddy, Curnier, & Elleberg, 2014; Rüfer et al., 2014). In contrast, high-intensity physical exercise leads to a considerable IOP rise (Dickerman et al., 1999; Vieira et al., 2006). There are different theories to explain the IOP rise during resistance exercise. For example, it has been documented that IOP changed transiently in parallel with blood pressure during isometric exercise. The increase in blood pressure and IOP has been speculated to be related to the strength of contraction and also to the size of muscle mass involved during exercise (Bakke et al., 2009). Therefore, the intensity and the metabolic demands of exercise seem to influence those IOP variations. In addition, other activities that involve changes in respiratory gas exchange, such as playing wind instruments, have shown to promote an IOP increment and this change was correlated with the degree of exhalation (Schuman et al., 2000). Similarly, Dickerman et al. (1999) reported that individuals producing maximal isometric contractions while holding their breath promote a mean IOP increment of 15 mm Hg, and Vieira et al., (2006) found that 4 repetitions of a bench press exercise lead to IOP increase, with greater IOP values when the participant held their breath.

Regarding the effect of the type of exercise performed on IOP changes, Rufer et al. (2014) found that upper limb exercises promoted a significant IOP increment whereas lower limb exercises did not induce any significant variation in IOP. It was suggested that this difference could result from an involuntary Valsalva maneuver while using the butterfly machine or, could be associated with increased facial muscle tension (facial congestion) during muscular effort (Silvia, Raczynski, & Kleinstein, 1984). We asked participants to avoid making Valsalva Manoeuvre during effort, but we cannot discard the possibility that is occurred unintentionally. Related to this assumption, it is also stated that executing intensive resistance exercise while lying down cause an IOP rise due to the consequences of the Valsalva Manoeuvre (Vieira et al., 2006). Both the supine posture and the performance of upper-body resistance training exercises contribute to the higher IOP rise when compared to the jump squat exercise with the same load. For example, when working out at 60 %RM, a mean IOP elevation of 0.89 mmHg and 3.94 mmHg was measured in jump squat and bench press respectively, which represents approximately 6% and 28% of baseline mean value. The cumulative effect of long-term intermittent IOP elevation during anaerobic exercise performance may result in glaucomatous damage as has already been shown by playing high resistance wind instruments (Schuman et al., 2000). Thus, exercising the upper-body in a supine position seems to be less desirable than resistance exercise in standing position or exercising the lower body for preventing IOP fluctuations. It has been stated in a previous investigation that exhausting effort could be a potential risk factor for the development and progression of glaucoma (Blair et al., 2004). However, the IOP variations in our study were observed over short periods of

time so we cannot establish the long-term effect on ocular health. Further research is required to clarify this.

Our results need to be replicated with glaucoma patients due to the possible disturbance in their autoregulation after postural changes (Galambos et al., 2006). Also, the technique for IOP assessment must be considered since repeated IOP measurements by applanation or indentation tonometry significantly diminish IOP on remeasurement, and this methodological bias can explain the IOP-lowering effect of exercise (Bakke et al., 2009). Our decision to use rebound tonometry to measure IOP was based on the fact that it has been demonstrated to show no learning effect is rapid and does not require the use of topical anesthetic (Pakrou, Gray, Mills, Landers, & Craig, 2008; Rüfer et al., 2014). The recent development of the contact-lens sensor for continuous IOP monitoring (Mansouri & Shaarawy, 2011) could offer a better alternative for recording the impact of physical effort on IOP. This technology avoids the inconvenience of IOP measurement devices that require the head and eyes to be motionless and has obvious practical advantages when outside the laboratory environment. It is our hope that future studies into the effect of resistance exercise and the long-term effect of strength training on IOP management will consider the effect of body position during resistance exercise, implement continuous IOP monitoring and include both female subjects and glaucoma sufferers.

In conclusion, the results of the present study indicate that the acute performance of basic resistance training exercises increases IOP. Regardless of the type of exercise (jump squat or bench press throw), the increase in the load was strongly associated with a linear increase in IOP. Interestingly, the increase in IOP was significantly higher in the bench press throw compared to the jump squat for the same relative load (%RM). The supine position of the bench press compared to the standing position of the squat could be responsible of the higher increase in IOP during the bench press throw. Based on these results, two basic recommendations can be provided to avoid undesirable IOP fluctuations in at-risk populations, involved in resistance training programs, particularly glaucoma patients or potential sufferers: 1) the use of low-moderate loads (< 50%RM), and 2) the avoidance of resistance training exercises performed in a supine position.

CHAPTER IV: MENTAL LOAD AND FATIGUE

Study 4. Intraocular pressure is sensitive to mental workload

Introduction

Intraocular pressure (IOP) is defined as the pressure exerted against the outer layers of the eyeball by its contents (Segen, 2006). This pressure is critical, being strongly involved in the development of glaucoma (Heijl et al., 2002; Levine et al., 2006). The autonomic nervous system controls IOP regulation, and the sympathetic-adrenal system plays a crucial role in aqueous humour inflow and outflow (Gherghel et al., 2004). Therefore, the estimation of IOP behaviour due to circadian variations (Mansouri et al., 2015), daily activities (Mansouri, Medeiros, & Weinreb, 2013; Risner et al., 2009; Yamamoto et al., 2008), and lifestyle (Cheung & Wong, 2007; Gherghel et al., 2004; Pasquale, Willett, Rosner, & Kang, 2010; Vera et al., 2016) must be taken into account to prevent or reduce the development and progression of glaucoma.

A great number of daily tasks require cognitive processing, mainly in work environments. When the mental workload increases by a longer time spent on task or higher task complexity, the central nervous system provides a greater supply of resources (Kong et al., 2005). Physiological measures are based on the concept that homeostatic disturbance can be measured on the structures sensitive to those changes (Ryu & Myung, 2005). In this perspective, Luft, Takase, and Darby (2009) found correlations between heart-rate variability (HRV) and cognitive performance, finding that HRV is an important marker of autonomic nervous system modulation. More recently, Luque-Casado et al. (2013 and 2015) showed the influence of cognitive processing and task-complexity manipulation on HRV. Thus, indices related to autonomic nervous system have proved to be sensitive to cognitive demand (Miyake et al., 2009; Trimmel, Fairclough, & Henning, 2009).

Due to the close relationship between ocular functioning and neurocognitive processes, and the fact that the eyes are considered part of the central nervous system, different oculo-physiological parameters are used as biomarkers of sympathetic-parasympathetic balance (Di Stasi et al., 2012; Wilson & O'Donnell, 1988). For example, Wang and Munoz (2015) demonstrated that various cognitive processes modulate pupil size from the projections of the superior colliculus. Regarding ocular accommodation, Davies, Wolffsohn, and Gilmartin (2005) found that rising cognitive demand impairs accommodative response. Similarly, Di Stasi et al. (2010 and 2011) concluded that saccadic peak velocity is affected by variations in mental workload, and they also demonstrated that changes in saccadic velocity indicate variations in sympathetic nervous system activation in naturalistic tasks (Di Stasi, Catena, Cañas, Macknik, & Martinez-Conde, 2013).

Previous works have speculated that IOP fluctuates after arousal variations as consequence of psychological stressors (i.e. mental arithmetic tasks) or induced-fatigue tasks (e.g. monotonous driving). The authors stated that those changes reflect the nervous system's activation state, and such variations cannot be attributed to any electromyographic changes in the surrounding eye muscle (Brody et al., 1999; Vera et al., 2016). The task complexity promotes autonomic nervous system changes. As IOP is not under voluntary control, we hypothesised that IOP could provide an accurate and unbiased measure of mental-task complexity by modulating the autonomic nervous system activity.

In this study, we investigated the effect of mental-task complexity on IOP, using for the control the classical index HRV for validation. Participants performed two cognitive tasks (on different days), but the mental-task complexity was manipulated using a mental-workload task (3-back) and the corresponding oddball version. We found that IOP alterations are directly linked to task complexity (higher increases with high task complexity). Our results incorporate evidence that IOP reflects autonomic effects after the manipulation of mental-task complexity.

Methods

Participants

The subject recruitment and experimental procedures for this study complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and permission was provided by the university Institutional Review Board (IRB) (Williams, 2008). A total of 15 healthy university student volunteers ($M = 22.27$ years old; $SD = 2.69$ years old) took part in this study, and all had given written informed consent prior to the study. We screened participants according to the follow inclusion criteria: (a) presenting static monocular visual acuity ($VA \leq 0$ log MAR in both eyes with their best optical correction (VA range: $-0.2-0$ log MAR; $M = -0.11$, $SD = 0.08$), (b) belonging to asymptomatic group at Conlon survey (≤ 24) (score range: $0-16$; $M = 7.29$, $SD = 5.57$) (Conlon et al., 1999), (c) not taking any medication (except contraceptives), and (d) being healthy (not suffering any current illness or mental disorder). Additionally, participants were asked to avoid alcohol and caffeine-based drinks 24 h and 12 h, respectively, before both experimental sessions, and to sleep regularly the night prior of attending the lab session. Participants reported their subjective levels of arousal before each session using the Stanford Sleepiness scale (Hoddes, Zarcone, & Dement, 1972) and all participants scored 3 or less (score range: $1-2$; $M = 1.54$, $SD = 0.51$), which has been used for screening in related experiments (Di Stasi et al., 2015; Vera et al., 2016). We excluded one participant from analysis due to HRV recording failure. Thus, here we analysed data from 14 out of 15 naïve participants (7 women,

age range: 19-29 years old; $M = 22.29$ years old, $SD = 2.79$ years old). As this study is the first of its nature, no power calculations were taken due to the lack of applicable data. We considered an appropriate sample size based on related studies, where statistically significant differences in ocular indices were found (Siegenthaler et al., 2014; Vera et al., 2016).

Stimuli and instruments

Mental-workload tasks and experimental conditions

The two experimental sessions were identical except for task complexity (see **Figure 11** for a schematic illustration). Participants performed three blocks of mental workload, each divided into five intervals consisting of 105 s of task trials, and a rest period of 15 s for the two first trials, 75 s for the third trial, and 15s for the two last trials of each cognitive block, resulting in 11 min long. All subjects performed 15 mental-task intervals, and this was therefore the total number of intervals considered to check cognitive involvement and performance.

The mental-workload task (a 3-digit load version of the N-back task) (Owen, McMillan, Laird, & Bullmore, 2005) consisted of a series of digits (1, 2, or 3), presented randomly, one at a time and at a rate of one digit every 2500 ms (each digit was presented for 1000 ms, and the inter-stimulus interval was 2000 ms). In each trial, the participants were asked whether the digit currently on screen was the same as the one presented 3 positions earlier, and they were requested to press a button each time a match was detected (participants did nothing if there was no match). This task thus requires keeping the three last digits in working memory (working-memory load), comparing every new digit with the earliest of them (checking), incorporating the new item and discarding the earliest one for further comparisons (updating). The task can be manipulated to raise or lower the working-memory load, depending on the number of digits the participant must keep in mind (3 in the current version of the task).

The oddball condition was designed to be perceptually identical to the 3-back task (Gomez & Perea, 2009; Perales, Verdejo-Garcia, Moya, Lozano, & Perez-Garcia, 2009). This condition allowed us to control the potential influence of stimulus-setting features (e.g. stimulus duration, inter-stimulus interval; see Luque-Casado et al., 2015). Before the task started, a randomly single digit (1, 2 or 3) was presented on the screen, and the participant was instructed to press the button every time the digit appeared on screen during that session, and to withhold the response for the other 2 digits. This task imposes little or no working-memory load, but uses exactly the same stimuli as the 3-back task, requires vigilance during the whole session, and takes the same rate of response (on average, one response/3 trials) (Luque-Casado et al., 2015).

To make responses, participants held a clicker on their dominant hand and a distinctive sound was used as feedback for each response. Cognitive tasks were displayed on a 19-in screen (1920 x 1080 pixels) situated 2.5 m from the participant’s eyes. Visual stimuli subtended 7 min of arc, which corresponds to 0.85 logMAR VA, and was thus clearly visible for any participant of this study. The experiment took place in a dimly lit laboratory. Illuminance of the room was quantified (in the corneal plane) with an illuminance meter (T-10, Konica Minolta, Inc., Japan), and kept constant throughout the entire experiment ($M = 62.59$ lux, $SD = 1.09$ lux).

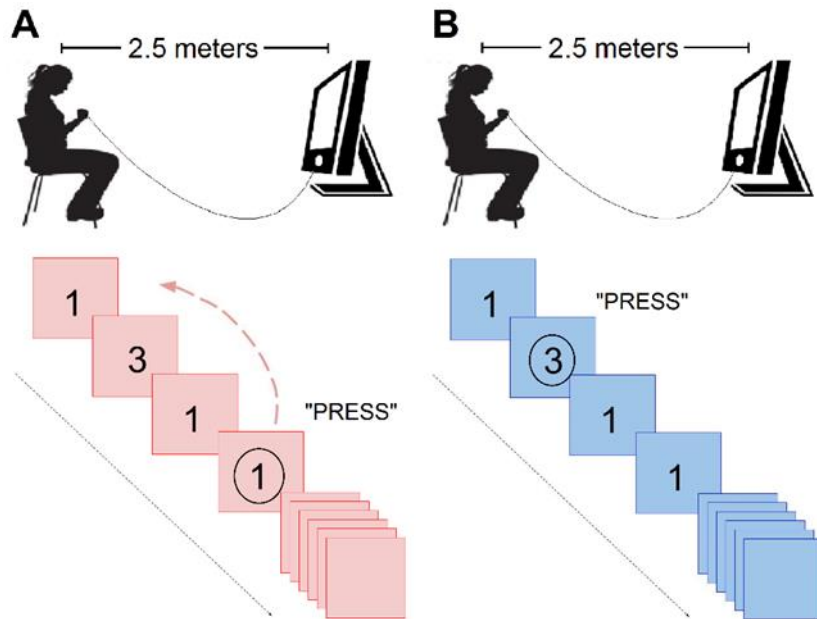


Figure 11. Schematic illustration of the experimental setting for the two conditions. On panel A (left side) the condition with high mental workload (3-back) is represented (in red). On panel B (right side) the oddball condition is shown (in blue). The two conditions were divided in three blocks of 11 min, with one-min break between blocks used for IOP assessment. Each block was divided in five trails of 105 s with a 15-s rest periods between trials, excepting a 75-s rest period after the third trail. For the 3-back task (panel A), participants read “press the button when the number on the screen matches the number presented three positions before”. In our illustration, participants should press the button since the number (1) matched with number presented three positions before. For the oddball condition (panel B), participants read the instructions “press the button when the number X (from 1 to 3, in our example the number randomly chosen was 3) appears on the screen”.

Intraocular pressure

IOP measurements were taken with an Icare Tonometer (Tiolat Oy, INC. Helsinki, Finland), and the order of the first eye measured (right, left) was randomized (Armstrong, 2013). Five measurements were taken from each participant: (1) immediately before the mental-workload task, (2) just after the first block, (3) just after the second block, (4) just after the third block, and finally (5) after 5 min of passive recovery. Participants were instructed to fixate on a distant target while the probe of the tonometer was held at a distance of 4 to 8 mm, and perpendicular to the

central cornea. Six rapidly consecutive measurements were performed against the central cornea and the mean reading displays digitally in mmHg on the LCD screen. The apparatus indicated whether differences between measures are acceptable or the SD is too large and a new measurement is recommended, and we always registered values with a low SD (ideal measure).

Heart-rate variability (HRV)

The polar RS800CX wrist device (Polar Electro Oy, Kempele, Finland) with an elastic electrode transmitter belt (Polar H3 heart-rate sensor) positioned on the chest was used to measure beat-to-beat (R-R) intervals at a sampling rate of 1000 Hz. A baseline recording was determined while participants were laid down in a quiet room for 6 min. During the three blocks of mental workload the heart signal was monitored, and finally a recovery measurement was made while participants remained seated for 5 min in the same quiet room.

Subsequently, data were transferred to the Polar ProTrainer Software and each downloaded R-R interval file was then further analysed using the Kubios HRV Analysis Software 2.0 (The Biomedical Signal and Medical Imaging Analysis Group, Department of Applied Physics, University of Kuopio, Finland) (Tarvainen et al., 2014). RR intervals which differed by more than 25% from the previous and subsequent R-R intervals were excluded, and those removed RR intervals were replaced by conventional spline interpolation so that the length of the data did not change. The time-domain method of analysis of the HRV data was used in this study, which is based on linear mathematical processes and on the mathematical calculation of the variations in the time occurring between beats. In this work, the parameter used to analyse HRV within the time domain were the high-frequency component (HF) in normalized units (nu), which is established between 0.15 and 0.4 Hz. HF values have proved to be a useful tool in the investigation of autonomic cardiovascular control (Luque-Casado et al., 2015; Reyes del Paso, Langewitz, Mulder, Van Roon, & Duschek, 2013). We used normalized units following the recommendations of Montano et al. (2009) for using HRV as a reliable marker of autonomic control. For analysis, we used 6 min for baseline recording, 11 min for each of three cognitive blocks, and 5 min of passive recovery after mental workload.

Cognitive-performance calculation

Regardless of the task (3-back or oddball) each response qualified as a hit (correct click), a false alarm (or commission error, incorrect click), a correct rejection (correctly non-clicking), or a miss (omission error, incorrectly non-clicking). We calculated the hit rate h (correct button pressings /total number of go trials) and the false-alarm rate f (incorrect button pressings/total number of no-go trials) for each block of the task (namely, the total number of intervals was divided in 3 equal blocks of 5 intervals (15 intervals in total), and h and f were computed for each of these

three block) to check the cognitive performance. Larger h and smaller f values indicate better response discriminability between go and no-go trials. A composite measure of discriminability can be computed as the arcsine of f minus the arcsine of h . The larger this difference of arcsines, the better the performance in the task (Perales, Catena, Shanks, & González, 2005).

Subjective questionnaires (SSS and NASA-TLX)

The Stanford Sleepiness Scale (SSS) is a 7-point Likert scale used to evaluate the self-reported activation of the individuals, which ranges from 1 “very active, alert or awake” to 7 “very sleepy” (Hoddes et al., 1972). The SSS was filled out upon arrival to the lab in both experimental sessions. Meanwhile, assessment of mental workload with the NASA-TLX scale was carried out after cognitive tasks. The NASA-TLX is composed of six subscales: Mental demand (How much mental and perceptual activity was required?), Physical demand (How much physical activity was required?), Temporal demand (How much time pressure did you feel due to the rate of pace at which the tasks or task elements occurred?), Performance (How successful do you think you were in meeting the goals of the task set by the experimenter?), Effort (How hard did you have to work to achieve your level of performance?), and Frustration level (How insecure, discouraged, irritated, stressed and annoyed vs. secure, gratified, content, relaxed, and pleased did you feel during the task? The participants had to score each subscale into 20 equal intervals anchored by a bipolar descriptor (e.g. Low/High), this score was multiplied by 5, resulting in a final score between 0 and 100 (Hart & Staveland, 1988).

Procedure

Participants took part in three sessions: (a) after signing the informed consent and visual questionnaires, participants underwent a monocular static visual-acuity assessment using a computerized monitor with the logarithmic letter charts employing the Bailey-Lovie design (Lovie-Kitchin, 2015) (VistaVision, Torino, Italy) at 5 m distance. Then, the participants were given instructions concerning the mental-workload task and NASA-TLX scale. Lastly, after a verbal explanation, participants were given 5 min to practice with both mental-workload tasks (3 back and oddball), so that all subjects were familiar with the procedure before the experiment. The second (b) and the third session (c) constituted the primary focus of the study in which two different mental-workload tasks with two levels of complexity were performed. Upon arrival to the lab, participants filled the SSS scale. Just afterwards, the resting HRV was recorded for 6 min, and the baseline IOP reading was taken continuously before mental effort. At this moment, participants started to perform the mental workload task while HRV was monitored, and IOP measurements were made just after each of the three blocks. When the mental effort was finished, participants filled the NASA-TLX scale, and rested for 5 min before the examiner took the last

IOP measurement. Two main experimental sessions were separated by a minimum of 24 h and a maximum of 48 h. Both visits were scheduled at the same time of the day to avoid diurnal fluctuations that affect arousal levels (Del Rio-Bermudez, Diaz-Piedra, Catena, Buela-Casal, & Di Stasi, 2014) and conducted in a counterbalanced order.

Experimental design and statistical analysis

The study followed a repeated-measures design. The measurement moment (pre, block 1, block 2, block 3, and recovery) and task complexity (3-back, oddball) were the within-subjects factors while IOP and HRV were the dependent variables. We also determined the participant's subjective mental workload via standardized questionnaires and cognitive-performance scores.

To test the effect of task complexity on IOP and HRV, a repeated-measures ANOVA was carried out with the measurement moment (pre, first block, second block, third block, and recovery) and task complexity (3-back, oddball) as the within-subjects factors. To ensure engagement in the mental workload task, we submitted the cognitive performance (difference of arcsines) measure to a 3 (block) x 2 (task complexity: 3-back/oddball) analysis of variance (ANOVA), with the two factors manipulated within-participants. Bonferroni correction was used for multiple comparisons. To analyse the effect of mental-task complexity on subjective measures (NASA-TLX), we performed a T-test for related samples, considering the task complexity as the within-subjects factor.

Results

Participants performed 33 min of mental workload with two different levels of complexity on two different days and in a counterbalanced manner, and we determined the effect of mental-task complexity on IOP and HRV. Also the subjective level of mental load was asked after tasks and cognitive performance were calculated from the entire tasks.

Cognitive-manipulation check

As in related research, we used the cognitive performance and subjective response to examine the effectiveness of task-complexity manipulation (Di Stasi et al., 2016; Di Stasi et al., 2014; Siegenthaler et al., 2014). The ANOVA showed a significant effect of task complexity, $F(1,13) = 57.967$, $MSE = 0.209$, $p < .01$, $\eta_p^2 = 1$. Neither the effect of measurement point (1-3) nor the task complexity x measurement point interaction proved significant, $F(2,26) = 0.319$, $MSE = 0.014$, $p = .69$, and $F(2,26) = 3.332$, $MSE = 0.068$, $p = .051$, respectively. The analysis of subjective response with NASA-TLX indicated the manipulation of task complexity, and

participants experienced higher levels of mental demand at the end of the 3-back task , 35.54 ± 12.25 , with respect to the oddball task 13.33 ± 4.68 , $t(13) = -7.552$, $p < .01$ (see **Figure 12**, panel A).

Effect of task complexity on IOP

For the IOP measurements, there was a significant effect of the interaction measurement moment x task complexity, $F(4,52) = 3.035$, $MSE = 2.019$, $p = .039$, $\eta_p^2 = .679$. No effects were found for task complexity and measurement moment, $F(1,13) = 0.571$, $MSE = 16.211$, $p = .463$ and $F(4,52) = 3.621$, $MSE = 2.262$, $p = .193$, respectively. As a result of the interactive effect, two separate one-way ANOVAs with the measurement moment (5) as factor were performed for each task complexity (3-back, oddball). A statistically significant effect was found for the measurement moment in the 3-back condition, $F(4,52) = 3.503$, $MSE = 2.646$, $p = .034$, $\eta_p^2 = .667$. The oddball condition was far from showing any effect for IOP, $F < 1$ (see **Figure 12**, panel B).

Effect of task complexity on HRV

A repeated measures ANOVA task complexity (2) x measurement moment (5) showed significant effects for the measurement moment of HF (nu), $F(4,52) = 5.292$, $MSE = 103.799$, $p < .01$, $\eta_p^2 = .881$. A marginally significant effect was found for the interaction load x measurement moment in the HF component, $F(4,52) = 2.432$, $MSE = 44.953$, $p = .067$. No effect was shown for the task complexity, $F < 1$. Then, two separate one-way ANOVAs with measurement moment as a factor (5) were carried out for the HF component for each task complexity (3-back, oddball), as we did with IOP. The analysis revealed a significant effect for measurement moment for the HF component in the 3-back session, $F(4,52) = 7.84$, $MSE = 48.669$, $p < .01$, $\eta_p^2 = .996$. No statistically significant differences were found for the oddball session, $F(4,52) = 1.455$, $MSE = 70.196$, $p = .235$, (see **Figure 12**, panel C).

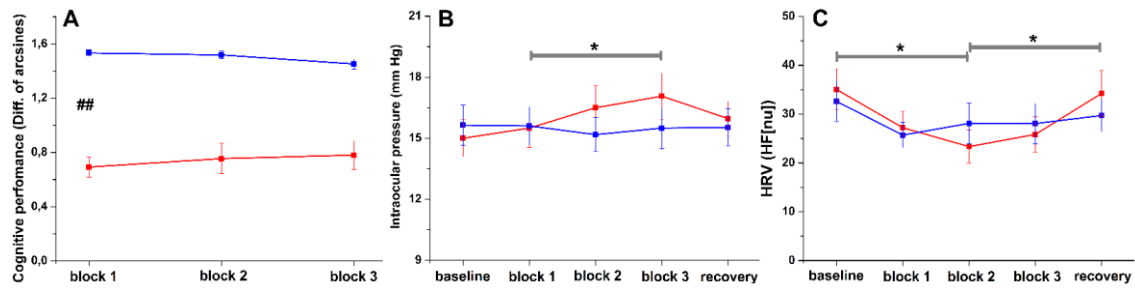


Figure 12. Effects of task complexity on the cognitive performance, intraocular pressure and HRV. (A) Cognitive performance (B) intraocular pressure and (C) HRV across participants at the two task-complexity levels. Data from the 3-back condition represented in red, and from the oddball task, in blue. In the panel (A) the cognitive performance for the three mental workload blocks are displayed, and higher scores indicate better performance. In the panel (B and C) the intraocular pressure and the HRV, respectively, show the effect of time on task and task complexity. The x-axis shows the measurement before mental workload, the three continuous blocks of mental workload, and the recovery measurement (5 min) for the panels (B and C). In the panel (C) higher values indicate higher autonomic control. * indicates statistically significant differences between the measurement moments represented with grey lines (corrected p-value < 0.05). ## indicates statistical differences between task-complexity levels (p-value < 0.01). Error bars represent the standard error (SE). All values are calculated across participants (n=14).

Discussion

IOP is sensitive to autonomic response to different demanding tasks such as physical exercise (Risner et al., 2009), sexual activity (Mansouri et al., 2013), and cognitive processing (Brody et al., 1999; Vera et al., 2016). Also, IOP changes because of circadian rhythms (Mansouri et al., 2015), body composition (Pasquale et al., 2010), and systemic diseases (Cheung & Wong, 2007; Gherghel et al., 2004). In particular, the effect of psychological stress on IOP has been demonstrated to respond to psychological stressors and induced-fatigue procedures due to autonomic effects (arousal variations) (Brody et al., 1999; Vera et al., 2016). Here, we examined how task complexity and time on task affect IOP and autonomic cardiovascular control (HF component of HRV) in two matched experimental sessions, where the only difference between the sessions was the mental workload due to task complexity. Our results show a cumulative and instantaneous effect of task complexity on IOP and HRV, a significant change for the most cognitively demanding task (3-back). Five min of recovery proved sufficient to return to baseline values.

A successful manipulation of task complexity has been corroborated with the analysis of cognitive performance and subjective responses (NASA-TLX). Cognitive performance was worse for the high task complexity, which indirectly proves that the high load task (3-back) is more difficult than the oddball task (Cárdenas et al., 2013; Galy, Cariou, & Mélan, 2012; Paas, Tuovinen, Tabbers, & Van Gerven, 2003). In this line, the NASA-TLX scores agree with the findings of

previous studies (e.g. Karavidas et al., 2010; Luque-Casado et al., 2015), which revealed that the execution condition promoted a heavier mental workload than did the oddball condition. Similarly, the autonomic response, measured by HRV, demonstrated differences between levels of complexity as has been described in previous research whereby a N-back task induced lower HRV than did the oddball version (Luque-Casado et al., 2015).

Since task complexity and time-on task have the potential to alter the nervous system's activation state (Di Stasi, McCamy, et al., 2013), it is plausible to expect that two different levels of task complexity would modify arousal levels in a different manner. Likewise, the autonomic innervation of the vertebrate eye is responsible for regulating the intraocular-pressure levels (Neuhuber & Schrödl, 2011), and thus central-nervous-system variations could strongly influence the IOP. Related works have proposed that the sleep-regulation centres (i.e. nucleus raphe magnus, nucleus raphe dorsalis, and locus coeruleus) and the superior colliculus, both in the reticular formation and cerebellum, are linked to eye-movement dynamics, pupil responses, accommodative response, and intraocular pressure changes as consequence of arousal variations (Di Stasi, McCamy, et al., 2013; Goldwater, 1972; Vera et al., 2016; Wang & Munoz, 2015). Moreover, we support the contention that high task complexity increases IOP due to a rise in nervous system's activation, as corroborated by the HRV analysis in the present study.

Blood-flow physiology is determined by the autonomic nervous system, among other factors (Appenzeller & Oribe, 1997). Due to a close relationship between the autonomic system and the cardiovascular system, variations in the nervous system's activation state will result in fluctuations in blood pressure and heart rate, as well as in IOP. (Faridi, Park, Liebmann, & Ritch, 2012; Gherghel et al., 2004; Vera et al., 2016). Along this line, Bakke et al. (2009) found that IOP increases parallel to the transient, continuous changes in systemic blood pressure during isometric exercise. As explained in a previous section [see Heart-rate variability (HRV)], HRV is an index of the interaction between the autonomic nervous system and the cardiovascular system (Pumprla et al., 2002). Based on all this evidence, in the present study we hypothesised that IOP is instantaneously affected by continuous mental workload. Thus, measuring IOP provides a simple means, similar to the way in which HRV has been used in previous studies (Luque-Casado et al., 2015), to assess mental workload in several fields of applied ergonomics.

Subjective scaling techniques are widely used but at the same time they are questioned, because they may not accurately estimate mental workload (Annett, 2002; Paas et al., 2003). Therefore, numerous studies have been conducted to find reliable and sensitive physiological biomarkers that objectively characterize the level of mental workload (Paas, Tuovinen, Tabbers, & Van Gerven, 2003). In this perspective, this work establishes a promising ocular candidate (IOP) to assess mental workload. With regard to the instrument employed, rebound tonometry may be an appropriate technique to measure IOP, which has been demonstrated to be an objective, easy,

rapid, and well-tolerated procedure to take it (Davies et al., 2006). However, other IOP measuring instruments (e.g. Goldmann aplanation tonometry, non-contact tonometry, etc.) require further investigation. Interestingly, recent development of contact-lens sensor based on the dimensional changes of the eye at the corneoscleral junction [for example, SENSIMED Triggerfish, Lausanne, Switzerland; see Mansouri et al., (2015) for more details] would allow IOP continuous monitoring out of a laboratory setting in cognitively demanding tasks. It is our hope that future studies will consider the effects of different cognitively demanding tasks on IOP in real-life scenarios, mainly in extreme situations (e.g. surgical procedures, flight operations, etc.).

In summary, IOP can reflect the cumulative effect of mental workload, suggesting that IOP depends on nervous system's activation state. These findings have potential impacts in the development of neuroergonomic tools to detect mental states in ecological settings.

Study 5. Accommodative response and intraocular pressure reveals driving fatigue

Introduction

Visual fatigue (i.e. asthenopia) can occur during prolonged working time that requires intense use of the eyes (Chase, Tosha, Borsting & Ridder 2009), as the oculomotor system makes continuous efforts to maintain accommodation, convergence, and direction of the gaze (Krupinski, Berbaum, Caldwell, Schartz, & Kim, 2010). Therefore, it is likely that prolonged driving time – a task mainly reliant on the visual system (Sivak, 1996) – might cause visual fatigue, including slowness of focus change, changes of pressure in the eye, and eyestrain (Ukai & Howarth, 2008). Indeed, recent studies using subjective measures have shown that visual fatigue symptoms might be a good indicator of impaired driving among sleepy drivers (Filtner et al. 2014). However, the use of self-reported surveys for evaluating visual fatigue symptoms present methodological caveats (e.g. individual heterogeneity) that can bias test scores (Wang & Xu, 2015). Moreover, self-reported visual discomfort might not be necessarily related to an objective impairment in visual functions (Sullivan, 2008). Thus, the question of whether driving time actually impacts visual function remains open.

Prolonged driving time represents a major cause of road fatalities (Di Stasi et al., 2015; Lee et al., 2016). It lowers driver's arousal and, consequently, impairs performance (Dawson, Searle, & Paterson, 2014). For this reason, international agencies are conducting extensive research in order to provide scientific-based methods to detect impaired driving (Marcus & Rosekind, 2016; National Highway Traffic Safety Administration, 2015). Visual neuroscience has demonstrated the utility of ocular parameters in detecting arousal variations in driving contexts (Di Stasi et al., 2015; Howard et al., 2014; Lee et al., 2016; Russo et al., 2003). Previous research has shown that prolonged driving – and other fatigue-related factors such as restricted sleep – alters the velocity of eyelid and saccadic movements as the result of non-optimal levels of arousal (Caffier, Erdmann, & Ullsperger, 2003; Di Stasi et al., 2012; Di Stasi et al., 2015; Howard et al., 2014; Jackson, Kennedy, et al., 2016; Jackson, Raj, et al., 2016; Johns, Tucker, Chapman, Crowley, & Michael, 2007; Lee et al., 2016; Wilkinson et al., 2013).

Non-optimal levels of arousal as a result of prolonged driving time might be caused by variations of the autonomic nervous system activity (Di Stasi et al., 2015; Wertheim, 1978). The autonomic nervous system innervates, amongst other structures, the ciliary body (muscle and processes) (Gilmartin, 1986) that controls for the accommodative response (AR, i.e. the ocular response that

allows people to see clearly at different distances) (Anderson, Glasser, Stuebinger, & Manny, 2009; Hinkley, Iverson-Hill, & Haack, 2014; Iwasaki, 1993) and the intraocular pressure (IOP, i.e. the tension exerted by the aqueous humor inside the eye as a result between its production and outflow) (Kiel, Hollingsworth, Rao, Chen, & Reitsamer, 2011; Nuyen & Mansouri, 2015). Therefore, prolonged driving time might affect AR and IOP response by modulating the autonomic nervous system activity. Previous work in non-driving contexts have demonstrated that arousal affects both AR and IOP (Ido, Tomita, & Kitazawa, 1991). For example, Saito and colleagues (1994) found that prolonged visual display terminal work (~4 hours) decreases AR (lower amplitude and velocity of accommodation). Reduction of the levels of arousal due to time-on-task (Wickens, 2008) might explain this result. In support of this explanation, recent work has shown that AR is impaired by central nervous system depressor drugs (e.g. benzodiazepines) (Chan et al., 2012; Speeg-Schatz et al., 2001). No study has investigated how prolonged visual-based tasks affect IOP, even though reductions in IOP have been obtained by lowering arousal levels through the ingestion of autonomic nervous system agents, such as parasympathomimetic drugs (e.g. Pilocarpine) (Toris, Zhan, Zhao, Camras & Yablonski 2001). Furthermore, increments in IOP have been obtained by increasing levels of arousal through external stressors (e.g. performing mental arithmetic tasks) (Brody et al., 1999). In considering all of the previous results that relate AR and IOP with arousal levels, it is plausible to expect that driving time, which prominently lowers arousal, also modulates AR and IOP. As AR and IOP are not under voluntary control, they could provide an accurate and unbiased measure of drivers' visual fatigue signs (contrarily to questionnaires) and could be used to prevent crucial impairments in driving performance.

In this study, we investigated the effects of prolonged driving time on AR and IOP. We recorded both parameters before and after a 2-hour driving session in a virtual scenario. We found that, after driving, both AR as well as IOP decreased. Our results represent an innovative step towards a valid and reliable assessment of fatigue-impaired driving based on visual fatigue signs.

Methods

Ethical approval

We conducted the study in conformity with the Code of Ethics of the World Medical Association (Declaration of Helsinki) (Williams, 2008). The experiment was carried out under the guidelines of the University of Granada's Institutional Review Board (IRB approval #24/CEIH/2015).

Written informed consent was obtained from each participant prior starting the study and they received a 30€ compensation.

Participants

Seventeen active drivers (5 women and 12 men, age [mean \pm statistical deviation, SD] 25.24 \pm 3.40 years), holding a valid driver license (years with a driver license [mean \pm SD]: 6.00 \pm 2.92 years), volunteered to participate in this study. Before starting the experiment, a board certified optometrist (JV) performed a routine evaluation to screen participants for any symptomatology, ocular pathology, as well as general conditions that could affect or mask AR and IOP variations. Hence, the inclusion criteria were 1) normal vision (visual acuity of ≤ 0 log MAR in each eye) 2) normal tonic accommodation level (accommodative lag of < 1.55 diopters (D) at 20 cm, the highest value in the normal range [Wang & Ciuffreda 2004]); 3) no significant uncorrected refractive error that could affect accommodation and vergence systems: myopia of < 0.50 D, astigmatism and anisometropia of < 1.00 D, and/or hyperopia of < 1.50 D (Chase, Tosha, Borsting & Ridder 2009); 4) low visual discomfort symptomatology, based on the scores of the Conlon visual discomfort survey (< 24) (Conlon et al., 1999). Furthermore, we excluded participants with any medical conditions (or under treatment with medications) that might cause visual alterations. Additionally, participants were instructed to abstain from alcohol and caffeine-based beverages for 24 h and 12 h, respectively, before the driving session. Finally, the participants had to get at least 7 h of sleep the night prior to the study. Also, for screening purposes, we measured subjective levels of arousal before the driving session using the Stanford Sleepiness Scale (Hoddes et al., 1972) (see Subjective questionnaires of perceived arousal and fatigue): no participants scored more than 3, had they done so they would have been excluded from further testing (Di Stasi et al., 2015). We excluded three participants because their accommodative lag was higher than 1.55 D at 20 cm. Two participants suffered from simulator sickness and did not finish the driving session. As a result, we analyzed data from 12 out of 17 participants (5 women and 7 men, age [mean \pm SD] 24.42 \pm 2.84 years). Owing to the lack of applicable pilot data – this study being the first of its nature – no power calculations were undertaken. The number of participants was considered appropriate based on a previous cohort, where statistically significant differences in the oculomotor metrics were found (Di Stasi et al., 2012).

Experimental design

A pre/post-test design was used to assess the impact of driving time on ocular parameters. The within-subjects factor was the *measuring session* (i.e. Pre-Driving vs. Post-Driving) and the dependent variables were drivers' AR (at five *accommodation distances*: 50cm [2D], 40cm [2.5D], 33cm [3D], 25cm [4D], and 20 cm [5D]) and IOP before and after the driving task. We also

recorded the participants' subjective levels of arousal and fatigue via standardized questionnaires (see Subjective questionnaires of perceived arousal and fatigue).

Stimuli and instruments

We developed a two-lane rounded rectangle virtual circuit using the OpenDS 2.5 software (OpenDS, Saarbrücken, Germany). Participants drove a mid-sized car for 2 hours around the circuit in sunny conditions without rest breaks and without any other traffic present (number of laps [mean \pm SD] 62.17 ± 2.62 , speed [mean \pm SD] 46.63 ± 1.97 km/h). Participants were seated on a comfortable car seat (PlaySeat®, Doetinchem, The Netherlands) and also used the Logitech G27 Racing Controller (steering wheel, gas and brake pedals; Logitech International S.A., Lausanne, Switzerland) to control the simulated car. Speedometer and tachometer gauges were shown in the bottom right of the screen. Rear and side mirrors were not displayed. Similar experimental settings – both software and hardware – have been successfully used to investigate drowsy driving (Isnainiyah, Samopa, Suryotrisongko, & Riksakomara, 2014; Lawoyin, Fei, & Bai, 2014; Lawoyin, Fei, Bai, & Liu, 2015). We used a video projector (EB-410W, EPSON Pty Ltd., Australia) to display the virtual circuit on a 1.32 x 1.63 m screen. To avoid visual fatigue caused by looking at the projected screen, we displayed the virtual scenario about 2.5 m from the driver's eyes (resulting in a view angle of $\sim 30^\circ$ vertically and $\sim 36^\circ$ horizontally) (Jaschinski, Heuer, & Kylian, 1999). The experiment took place in a dimly lit laboratory. During the entire experimental session, we controlled for room illumination (corneal plane), temperature, and background noise (~ 24 lux [Illuminance meter T-10, Konica minolta, Inc., Japan], $\sim 25^\circ\text{C}$ [Arduino Uno digital thermometer], and ~ 52 dB [Sound Level Meter DSL-330, Tecpel Co Ltd., Australia], respectively).

Subjective questionnaires of perceived arousal and fatigue

We asked participants to fill in two questionnaires pre and post the driving simulation in order to evaluate the effectiveness of the fatigue-inducing manipulation: the Stanford Sleepiness Scale (SSS) and an adapted version of the Borg Rating of Perceived Exertion Scale (BORG) were utilized. The SSS provides a global measure of how alert a person is feeling, ranging between 0 and 7 (Hoddes et al., 1972). It contains seven statements ranging from “Feeling active, vital, alert, or wide awake” (score 1) to “No longer fighting sleep, sleep onset soon, having dream-like thoughts” (score 7). The BORG indicated the level of perceived exertion associated with a task. It consists of a numerical scale (ranging from 6 to 20) anchored by “Not exertion at all” (score 6) to “Maximal exertion” (score 20) (Borg, 1998).

Recordings systems and analyses

Intraocular pressure

We measured IOP values from both eyes just before/after the driving simulation, using the Icare rebound tonometer (TA01; Tiolat Oy, Helsinki, Finland). Participants, during the test, fixated on a distant target while the probe of the tonometer was held at a distance of 4 to 8 mm from the eye, perpendicularly to the central cornea. We randomly chose the first eye to measure (Armstrong, 2013). Six consecutive measurements were taken for each eye, leaving a 30-sec interval between them. To enhance internal validity, we took these measurements twice. For each measurement, the highest and the lowest values were automatically discarded. Thus, we calculated the average Pre/Post-Driving IOP value from the remaining sixteen IOP measurements (four values per eye - taken twice- per measuring session).

Accommodative response

We measured dynamic AR values just before/after the driving simulation, using the Grand Seiko WAM-5500 open field autorefractor (Grand Seiko Co. Ltd., Hiroshima, Japan). To obtain a robust dynamic AR, we performed a static refractive test (AR baseline) before commencing the driving simulation. We asked participants to look at a target positioned 3m from their eyes while resting their forehead and chin on the head/chin support. Participants viewed the target monocularly through a 12.5 x 22 cm open-field beam-splitter, while the contralateral eye was covered with the instrument's occluder. We repeated this procedure ten times for both eyes. Then, just before and after the driving simulation, we performed a dynamic refractive test at 5 accommodation distances (50, 40, 33, 25, and 20 cm), recording AR binocularly continuously for 31-sec (5 Hz sampling rate). We asked participants to look at a 2 cm high-contrast (Michelson = 79%) five-point black star target presented on a white background card. This type of target contains a broad range of spatial frequencies, providing detail at a variety of orientations and an appropriate cue for central fixation (Kruger, Stark, & Nguyen, 2004). The base luminance of the target was 31 cd m⁻² and illumination condition was ~22 lux. We displayed the target at five locations (accommodative demand, distances measured, and viewing angles): 1) 2D, 50cm, 2.29°; 2) 2.5D, 40cm, 2.86°; 3) 3D, 33cm, 3.47°; 4) 4D, 25cm, 4.58°, and 5) 5D, 20cm, 5.73°, with a 60 second break between measures. For data analysis, we first identified and removed data points that were more than ± 3 SD away from the mean spherical refraction value (Tosha, Borsting, Ridder, & Chase, 2009). To remove transient effects from the stimulus onset (Di Stasi, McCamy, et al., 2013), we discarded data from the first second of each 31 second trial. Then, we performed the analysis on the remaining 30 seconds. As measure of AR, we used the accommodative lag (i.e. the amount of under-accommodation), calculated as in Poltavski and colleagues (2012) by subtracting from the target distance (in our case 2D, 2.5D, 3D, 4D, and 5D), the mean point of focus during dynamic testing and the baseline static refraction value. (Note: AR is obtained in binocular viewing, but the Grand Seiko WAM-5500 permits only to record data from one eye at the time. Based on the

results from the static refractive testing, we selected the eye with the lower spherical equivalent error [see above]).

Procedure

After signing the consent form, participants filled in the SSS and BORG scales and we measured the AR and the IOP. Then, after a five-minute familiarization session, the driving simulation started. We instructed participants to follow the usual traffic rules and to keep the car mostly in the right lane. Maximum speed limit was 60km/h. During the entire simulation, the experimenter did not communicate with participants, although they were constantly monitored through an observation window behind the car seat. The length of the simulation was similar to the maximum driving time recommended for professional drivers before a mandatory break (i.e. 2 hours) (Vehicle and Operator Services Agency, 2009). After the simulation, participants filled in the same scales and we measured the AR and IOP again. We measured IOP while the participants were seated in the car seat, i.e. right before and after the driving simulation started and ended. In order to avoid diurnal fluctuations (e.g. afternoon dip) that affect arousal levels (Del Rio-Bermudez et al., 2014) – and consequently could affect IOP and AR – all experimental sessions started at 9 am and finished before noon (12 pm). Finally, to avoid an end-spurt effect-reactivation – that occurs when people know they are approaching the end of a task (Bergum & Lehr, 1963) – participants were not informed of the duration of the driving simulation.

Statistical analysis

To analyze the effect of prolonged driving time on AR, we conducted a repeated-measures ANOVA with the accommodation distance (2D, 2.5D, 3D, 4D, and 5D) and measuring session (Pre-Driving vs. Post-Driving) as within-subjects factors. We used the Bonferroni-correction for multiple comparisons. To analyze the effects of prolonged driving time on IOP and subjective measures (SSS and BORG scores), we also performed separate T-tests for related samples, considering the measuring session as the within-subjects factor.

Results

We determined the effect of prolonged driving time on drivers' ocular parameters, specifically on AR and IOP. Participants drove for 2 hours without any rest in a simulated road circuit. Before and after the driving session, we measured AR and IOP responses, together with the subjective levels of arousal and fatigue.

Effectiveness of the fatigue-inducing manipulation

To examine the effectiveness of the fatigue-inducing manipulation, we analyzed responses to the questionnaires (SSS and BORG scales). The subjective results indicated the successful manipulation of driving-induced fatigue (i.e. prolonged driving time): participants experienced lower levels of arousal and higher levels fatigue at the end of the 2-hour drive, $t(11) = 6.1, p < 0.001$; $t(11) = 4.2, p < 0.001$, respectively (see **Table 8**).

Intraocular pressure and accommodative responses

The average IOP decreased after the 2-hour drive, $t(11) = -2.5, p = 0.03$ (see **Figure 13A**). The mean accommodative lag increased (AR decreased) after the 2-hour driving session, $F(1, 11) = 16.4, p < 0.001$ (see **Figure 13B** and **Table 8**). Nearest distances (3D, 4D, and 5D) induced higher decreases in AR only after the driving session (all corrected p -values < 0.05 ; interaction between measuring session x accommodation distances, $F(4, 44) = 2.3, p = 0.07$; accommodation distances, $F(4, 44) = 1.7, p = 0.16$).

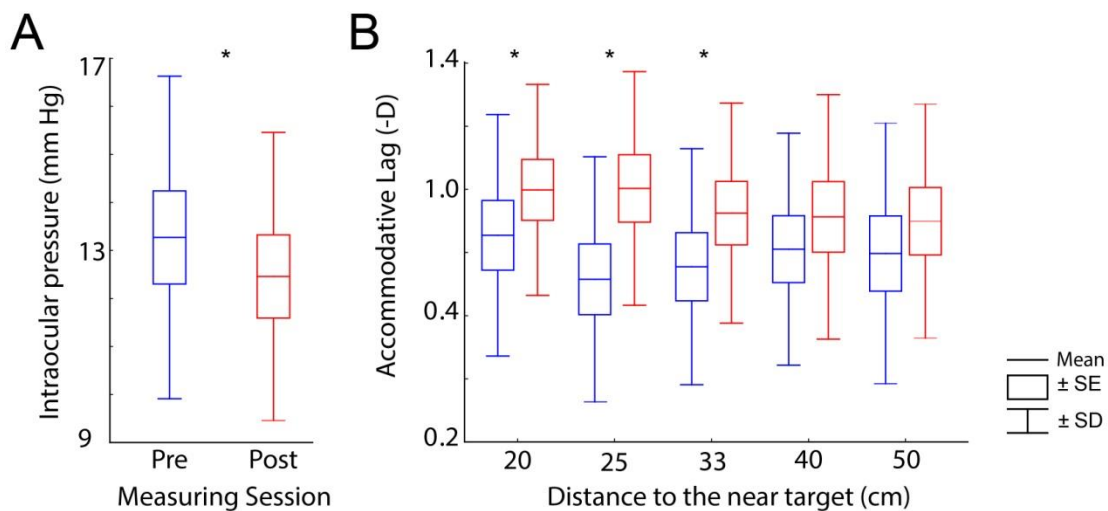


Figure 13. A) Effects of driving time on the intraocular pressure. B) Effects of driving time on the accommodative response. Average accommodative lag for each distance to the near target before and after driving session. The accommodative lag indicates the amount of under-accommodation, i.e. the inaccuracy of the focusing system. Here, higher values indicate lower accuracy. The accommodative lag is represented as a positive value for graphical purposes (diopter [-D]). A and B) Data from the Pre-Driving measure are indicated in blue and, from the Post-Driving measure, in red. * indicates statistically significant differences between the measuring sessions (corrected p -values < 0.05). Error bars represent the Standard Deviation (SD) and boxes represent the Standard Error (SE). Both values are calculated across participants ($n = 12$).

Table 8. The effect of prolonged driving time on ocular parameters and subjective measures. Average and standard deviation of the accommodative lag for each distance, intraocular pressure, and subjective ratings of arousal (SSS) and fatigue (BORG) before and after the 2-hour driving session. For the accommodative lag, the error in the accuracy of the accommodative system, lower values – in diopters – indicate higher levels of inaccuracy. For SSS and BORG scales, higher scores indicate lower arousal and higher perceived levels of fatigue, respectively.

Ocular Parameters	Pre-Driving	Post-Driving
	M (SD)	M (SD)
IOP (mmHg)*	13.27 (3.36)	12.45 (3.00)
ALag 20 cm (D) *	-0.85 (0.38)	-1.00 (0.33)
ALag 25 cm (D) *	-0.72 (0.39)	-1.00 (0.37)
ALag 33 cm (D) *	-0.74 (0.40)	-0.92 (0.35)
ALag 40 cm (D)	-0.81 (0.37)	-0.91 (0.40)
ALag 50 cm (D)	-0.80 (0.41)	-0.90 (0.37)
Subjective measures	Pre-Driving	Post-Driving
	M (SD), range	M (SD), range
BORG*	7.92 (1.51), 6-11	12.67 (2.96),7-17
Score range: 6-20		
SSS*	2.17 (0.72), 1-3	3.75(1.14), 2-6
Score range: 0-7		

Note. ALag=Accommodative lag; BORG=Borg Rating of Perceived Exertion Scale; D=Diopter^Ψ; IOP=Intraocular pressure; M=Mean; SD=Standard deviation; SSS=Stanford Sleepiness Scale.

* $p < 0.05$

Ψ: Unit of measurement of the dioptric power of a lens (m^{-1})

Discussion

Prolonged demands on the oculomotor functions might lead to a deterioration of visual performance. As the information relevant to driving is predominantly visual (Sivak, 1996) and because drivers are most of the time focusing and refocusing between the road and the dashboard or near and far traffic (Maravelias, 2015), we hypothesized that prolonged driving time would significantly impact ocular parameters. We found that the AR and the IOP significantly decrease with driving time, whereas fatigue levels increase. These results support the idea that visual fatigue is actually induced during prolonged driving sessions and it can be objectively measured through the AR and the IOP. Although the role of visual fatigue might be relevant in the context of driving safety (Sullivan, 2008), no research to date has investigated the effect of driver fatigue on AR and IOP responses. Prolonged driving time affects ocular parameters as it might reduce operator’s arousal levels (Di Stasi, McCamy, et al., 2016). In fact, recent articles studying saccadic and eyelid dynamics have found a velocity reduction as the level of driver fatigue increases (Di Stasi, Catena, et al., 2013; Di Stasi et al., 2012; Di Stasi, McCamy, et al., 2016; Di Stasi et al., 2015; Howard et al., 2014; Jackson, Kennedy, et al., 2016). In line with this working hypothesis, previous studies have explained changes in AR and IOP by the variation of person’s levels of activation (specifically, variations in sympathetic nervous system activation), either due to time-on-task (Saito et al., 1994), circadian variations (Liu et al., 2011), sleep stages (Faridi et

al., 2012), or sedative medication (Holve, 2012). Interestingly, the changes found here in both AR and IOP after two-hours of driving exhibit a similar tendency to those changes observed in AR (Campbell et al., 2001; Hogan & Gilmartin, 1985; Miller et al., 1986; Zoethout, Delgado, Ippel, Dahan, & Van Gerven, 2011) and IOP (Buckingham & Young, 1986; Flom et al., 1975; Green, 1998; Tomida, Pertwee, & Azuara-Blanco, 2004) after alcohol or cannabinoids consumption. Therefore, an arousal-based explanation to changes in AR and IOP is quite plausible.

Since we designed an extremely monotonous and predictable virtual simulation and the experiment was conducted in a darkened and sound-proof environment, it is possible that variations in AR and IOP were related to the reduction of the levels of arousal, similar to those levels observed when a driver falls asleep (Dawson et al., 2014). Sleep-regulation centres (i.e. nucleus raphe magnus, nucleus raphe dorsalis, and locus coeruleus) play an important role in the AR response (Schor et al., 1999) and IOP regulation (Kiel et al., 2011). Lower arousal levels should inhibit connections between the sleep-regulation centres and the superior colliculus, both in the reticular formation, and cerebellum (Di Stasi, McCamy, et al., 2013). Thus, changes in the AR may arise at the level of the excitatory connection from hypothetical arousal neurons to the lateral suprasylvian area, projected mainly to the rostral pole of the superior colliculus (rSC), and from the rSC through the Edinger-Westphal nucleus to modify accommodation (Suzuki, 2007). Lower arousal levels also cause pupil constriction (Wang & Munoz, 2015) and directly affect aqueous humor outflow (Brubaker, 2003). Changes in the aqueous humor outflow – through the trabecular meshwork, the canal of Schlemm, and the collector channels (Brubaker, 2003) – might have caused IOP variations with increased driving time.

One may wonder if the present changes in IOP and AR might have resulted from the effects of diurnal fluctuations or the impact of repeated measurements (i.e., cumulative effect). Firstly, we specifically controlled for the time of the day: we ran all experimental sessions – one participant per day – within the same temporal window and always ending the post-driving measurement session before noon. Moreover, a modulation of IOP and AR caused by diurnal fluctuations of the arousal seem unlikely. Prior investigations did not find changes in IOP and AR over the same time period tested here (9 am-noon) (Fisher, Ciuffreda, Tannen, & Super, 1988; Heron, Smith, & Winn, 1981; Johnson, Post, & Tsuetaki, 1984; Krumholz, Fox, & Ciuffreda, 1986; Liu et al., 2011; Liu et al., 1998; Mansouri & Shaarawy, 2011; Rosenfield, Ciuffreda, Hung, & Gilmartin, 1993). Secondly, a cumulative effect in both AR and IOP is highly improbable. Prior research demonstrated that a ~5-minute interval between measurement sessions is enough to avoid stressing the ocular motor system (Brody et al., 1999; Hasebe, Graf, & Schor, 2001; Liu et al., 1999; Richter, Zetterberg, & Forsman, 2015). For all of the above, it is plausible to infer that the IOP and AR decrements found here may arise at the level of the adrenergic activity (Bill, 1975),

which also plays an important role for the regulation of sleep/wake states (Ouyang, Hellman, Abel, & Thomas, 2004), and not to diurnal fluctuations of the arousal or a cumulative effect due to the measuring procedure.

The current study provides original data on the validity of AR and IOP as safety indices in driving. However, the lack of a control condition/group may be a limitation to our results. It is our hope that this study will spur further research on the effects of fatigue-related factors (including those derived from restricted sleep and circadian fluctuations) on IOP and AR in complex and ecological real settings, and will encourage the use of basic research in the service of the design of driver assistance systems (Di Stasi et al., 2010).

Conclusions

International departments of transportation limit the maximum driving time for each journey/week for passenger-carrying drivers (Vehicle and Operator Services Agency, 2009), however, the effectiveness of these regulations can be placed into question for several reasons (Haworth, 1995); which includes the omission of important factors that affect driver performance, for example, his/her levels of fatigue (i.e. arousal) (Del Rio-Bermudez et al., 2014; Di Stasi et al., 2015). Unfortunately, to date there is not a testing device (cf. the breath analyzer for alcohol levels) able to detect driver fatigue variations. Our results suggest that AR and IOP might be used as biomarkers of driver fatigue to enhance road safety strategies. As a result, our findings have a possible impact on the development of a valid and feasible tool to detect driver fatigue based on visual fatigue signs, and, moreover, suggest that ocular physiological responses have the potential to objectively signal the nervous system's activation state (either in relation to fatigue, drugs and alcohol consumption, or sleep restriction).

Due to the limitations in administering the test out of a laboratory setting, AR and IOP cannot be currently used as a fit-for-duty test. However, recent technology developments in ocular telemetrics for IOP continuous monitoring (for example, SENSIMED Triggerfish, Lausanne, Switzerland; see De Smedt et al. (2012) for more details) could lead to a driver fatigue monitoring system based on wearable devices in the future, similar to those fatigue detectors based on the eyelid behavior (e.g. Optalert, Cremorne, Australia, see Jackson et al. (2016) for more details). Further studies are required to determine whether IOP and AR might provide useful measures of driver fatigue in real settings in relation to factors other than time-on-task, such as evaluating the effects of restricted sleep (Howard et al., 2014) or circadian rhythms (Del Rio-Bermudez et al., 2014).

Study 6. A novel ocular index to assess the effect of cognitive processing

Introduction

A great amount of daily tasks require cognitive effort in different occupational settings such as learning at the school, public professional oppositions, surgical interventions, military operations, team sport games, among many others. In addition to the widely used subjective scaling techniques (Hart & Staveland, 1988; Nygren, 1991; Paas et al., 2003), numerous studies have been conducted to find reliable and sensitive physiological biomarkers that objectively characterize the level of mental workload (e.g., Paas et al., 2003). These physiological techniques include systemic physiological measures as heart activity (e.g., heart rate variability) (Durantin, Gagnon, Tremblay, & Dehais, 2014; Luque-Casado et al., 2015), near infrared spectroscopy (Durantin et al., 2014), brain activity (Di Stasi et al., 2015; Käthner, Wriessnegger, Müller-Putz, Kübler, & Halder, 2014) or hormonal changes (Qi, Gao, Guan, Liu, & Yang, 2016). Due to the fact that ocular functioning is tightly linked to neurocognitive processes, researchers have drawn their attention to ocular variables as potential objective biomarkers of these processes. So that, pupillary responses (De Gee, Knapen & Donner 2014, Klingner, Tversky & Hanrahan 2011, Wang & Munoz 2015), blink rate (Gowrisankaran, Nahar, Hayes, & Sheedy, 2012; Rosenfield, Jahan, Nunez, & Chan, 2015), accommodative response (Davies et al., 2005; Vera et al., 2016), intraocular pressure (IOP) (Brody et al., 1999; Vera et al., 2016) or saccadic eye movements (Di Stasi, Antolí & Cañas 2011, Di Stasi et al. 2013) have been well-documented.

Although pupil size has been demonstrated to show a positive correlation with increasing cognitive processing demand (De Gee, Knapen & Donner 2014, Klingner, Tversky & Hanrahan 2011, Wang & Munoz 2015), the pupil is directly dependent on the illumination level, which leads to ceiling effects in dim surroundings (Wang & Munoz, 2015). Also, controversial findings have been obtained about ocular accommodation behavior during these processes (Bullimore & Gilmartin, 1988; Davies et al., 2005; Jainta, Hoormann, & Jaschinski, 2008; Vera et al., 2016) and scarce investigations have been addressed to test the effect of mental tasks on IOP (Brody et al., 1999; Vera et al., 2016). In addition, these physiological parameters are closely linked and interdependent (Brubaker, 2003; Read et al., 2009), therefore it is difficult to independently control them in ecological conditions. Moreover, it could be logical to search a new ocular index which include these interactions and is sensitive to mental demanding tasks.

Ocular aberrations reflect the optical quality based on the ocular elements such as the anterior and posterior corneal surfaces, the crystalline lens, and the aqueous and vitreous humor. Wavefront aberrations refer to the deviations of a wavefront exiting the pupil after progressing through the

optics of the tested eye when compared to a reference wavefront that is aberration free. The most common method for describing the wavefront error of the eye is the normalized Zernike polynomials expansion (Thibos et al., 2002), and they represent the relative contribution of a specific Zernike mode to the total root-mean-square (RMS) error as well as the amount of deviation across the wavefront plane attributable to that specific aberration or mode (Pepose & Applegate, 2005). RMS is the deviation of the wavefront from a plane wavefront represented as a single digit (in microns) and RMS can be determined individually for lower or higher order aberrations or it can be calculated for the entire wavefront (Dai, 2008). The development of wavefront sensor (e.g the Shack-Hartmann aberrometer) allows the rapid, accurate, repeatability and objective measurements of ocular aberrations (Thibos & Hong, 1999). The higher the RMS wavefront error, the larger the wave-front aberration and the worse the optical quality.

In fact, ocular aberrations are affected by variables that reflect the activity of the autonomous nervous system (ANS), such as pupil size, accommodation and intraocular pressure (Brody et al. 1999, Davies, Wolffsohn & Gilmartin 2005, De Gee, Knapen & Donner 2014, Klingner, Tversky & Hanrahan 2011, Vera et al. 2016, Wang & Munoz 2015). In this line, we consider that this parameter could be used to evaluate the effect of mental workload or predict the level of autonomic activation. To date no study has assessed the ocular optical quality, in terms of ocular aberrations, under conditions of cognitive stress. We hypothesize that the evolution of the measurements of ocular aberrations could indicate changes in the activity of the autonomous nervous system as consequence of cognitive processing.

In this study, we measured ocular aberrations with a Shack-Hartmann wave-front sensor in a young adult population that performed two perceptually matched mental tasks (in different days) but with different level of mental complexity. Each subject served as his or her own control. One task was designed to produce a moderate/high level of working memory load (3-back), whereas the other one was the corresponding oddball version. Zernike coefficients up to the eight order were studied and high order aberration (HOA), spherical (SA), coma (CA), trefoil (TA), and astigmatism (AA) RMSs were calculated. Thus, to aid understanding of the actual changes it has been desirable to consider these effects for both mental tasks at four measurement moments and under natural pupil diameter and considering three constant pupil diameters (5, 4.5 and 4 mm).

Methods

Participants and ethical approval

The study was approved by ethics committee at University of Granada and the research followed the tenets of the Declaration of Helsinki (Williams, 2008). The nature of the study was explained to the participants and written, informed consent was obtained. Firstly, fourteen volunteers were enrolled in this study. Then, we screened participants to accomplish the follow inclusion criteria: (a) presenting static monocular visual acuity ≤ 0 log MAR in both eyes with their best optical correction, (b) belonging to asymptomatic group at Conlon (Conlon et al., 1999) and CISS (Borsting, Chase, & Ridder, 2007) surveys and not presenting any accommodative and binocular dysfunction (c) not taking any medication (except contraceptives), and (d) being healthy (not suffering any current illness or mental disorder), and (e) score ≤ 3 on the Stanford Sleepiness Scale (SSS), which measure subjective levels of arousal and fatigue, before each of the two main experimental sessions (Hoddes et al., 1972).

Autorefractometry was performed and the patient's previous clinical records were available at the time of testing and were used as a starting point for subjective refraction in most cases. Subjective refraction was conducted using a Snellen letters chart at six metres on both eyes of each subject by the same investigator (JV) and was performed using a trial frame and back vertex distance of 12 mm. The endpoint criteria were maximum plus sphere and minimum minus cylinder power maintaining the best visual acuity, which was recorded in logMAR (Lovie-Kitchin, 2015). Following the recommendations given by Scheiman and Wick (2008) respect to methodology and normative data, the amplitude of accommodation and accommodative response were evaluated to check the accommodative function with the push-up technique and monocular estimate method (MEM) retinoscopy respectively. Similarly, to test the binocular function, the near point of convergence, the fusional vergences (negative and positives) and near stereoacuity were tested. The push-up technique, the smooth vergence testing, and the Randot Stereotest were used, respectively. All participants accomplished the inclusion criteria established in the present study.

Participants were instructed to abstain from alcohol consumption 24 h and from caffeine-based drinks 12 h before each experimental session, and must have at least 7 h of sleep the night prior to the study. We excluded two participants because one of them reported sickness during the experimental session and failures during data collection for another participant. Thus, here we analyzed data from a total of twelve naive participants (mean \pm SD; age: 22.27 ± 2.69 years, 5 women, 7 men).

Procedure

Subjects took part in three sessions: (a) after signing the inform consent and filling visual questionnaires, the participants were given instructions about the mental workload tasks and the NASA-TLX scale. Lastly, after verbal explanation, participants were given five minutes to practice with both mental workload tasks (3-back and oddball), so that all subjects were familiar with them before the commencement of the study. All subjects performed the mental workload tasks with best spectacle correction. The second (b) and the third session (c) constituted the primary focus of the study in which two mental workload tasks with different levels of complexity were performed. These were separated by a minimum of 24 h and a maximum of 48 h and both sessions were scheduled at the same time of the day to avoid diurnal fluctuations that affect arousal levels (Del Rio-Bermudez et al., 2014) and carried out in a counterbalanced order (see **Figure 14**).

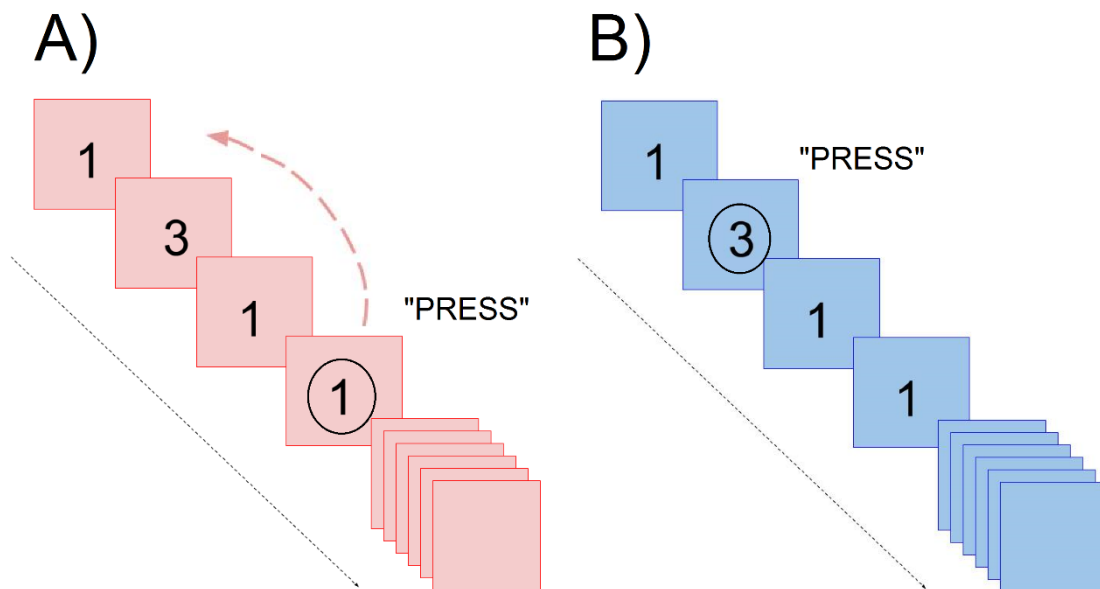


Figure 14. Schematic illustration of the experimental setting for the two conditions. On panel A (left side) the condition with high mental workload (3-back) is represented (in red). On panel B (right side) the oddball condition is shown (in blue). Mental workload tasks were divided in intervals of 105 s long with a 15-s rest periods between trials, excepting a 75-s rest period after the third trail. This sequence was maintained for the entire experimental session. For the 3-back task (panel A), participants read “press the button when the number on the screen matches the number presented three positions before”. In our illustration, participants should press the button since the number (1) matched with number presented three positions before. For the oddball condition (panel B), participants read the instructions “press the button when the number X (from 1 to 3, in our example the number randomly chosen was 3) appears on the screen”.

Stimuli and instruments

The two experimental sessions were identical except from mental workload task level implemented (3-back, oddball). Participants performed 33 minutes of mental workload displayed on a 19-in screen (1920 x 1080 pixels) situated 2.5 m from the participant’s eyes. Visual stimuli

subtended 7 min of arc, which corresponds to 0.85 logMAR VA, and was thus clearly visible for any participant of this study. Mental workload tasks were interrupted for one minute at the minute 11 to obtain ocular aberrations measurements. To make responses, participants held a clicker on his dominant hand and a distinctive sound was used as feedback for each response. The experiment took place in a dimly lit laboratory. Illuminance of the room was quantified (in the corneal plane) with an Illuminance meter (T-10, Konica Minolta, Inc., Japan), and kept constant during the entire experiment [*mean* \pm *SD*: 62.59 \pm 1.09 lux].

Mental workload tasks were divided in intervals consisted of 105s long, and a rest period of 15s for the first two intervals and 75s for the third one. This sequence was maintained during the entire session. All subjects performed 15 mental workload task intervals, and this was therefore, the total number of intervals considered to check cognitive involvement and performance.

Mental workload tasks

The mental workload task (a 3-digit load version of the N-back task, Owen et al. 2005) consisted of a series of digits (1, 2, or 3), presented randomly, one at a time and at a rate of one digit every 2500 ms (each digit was presented for 1000 ms, and the inter-stimulus interval was 2000 ms). In each trial, participants were asked if the digit currently on screen was the same as the one presented 3 positions earlier, and press a button every time a match was observed (participants did nothing if there was no match). This task thus requires keeping the three last digits in working memory (working memory load), comparing every new digit with the earliest of them (checking), incorporating the new item and discarding the earliest one for further comparisons (updating). The task can be manipulated to raise or reduce working memory load, depending on the number of digits the participant must keep in mind (3 in the current version of the task).

The oddball condition was designed to be perceptually identical to the 3-back task (Gomez & Perea, 2009). This condition allowed us to control the potential influence of stimulus setting features (e.g. stimulus duration, inter-stimulus interval, see Luque-Casado et al., 2015). Before the task started, a single digit (1, 2 or 3) was presented on screen, and the participant was instructed to press the button every time that digit appeared on screen during that session, and to withhold the response for the other 2 digits. This task imposes little or no working memory load, but uses exactly the same stimuli as the 3-back task, requires vigilance during the whole session, and the same rate of response (on average, one response/3 trials, Luque-Casado et al. 2015).

Ocular aberrations

Wavefront aberrations were measured before mental workload tasks, right after eleven minutes of mental workload, after finishing the 33 minutes of the mental workload, and after 10 minutes of passive recovery. Aberrometry was performed on the undilated pupil under mesopic conditions without any cycloplegia or mydriasis by the OPD Scan III (Nidek Inc., Tokyo, Japan). The OPD-

Scan III is a five-in-one true refractive workstation combined with a topographer, wavefront aberrometer, keratometer, and pupillometer, whose repeatability and accuracy have been contrasted in previous studies (Gifford & Swarbrick, 2012; Visser et al., 2011). Combined wavefront aberrometry and corneal topography can differentiate between aberrations caused by the anterior cornea or by the internal ocular system. Total ocular aberrations are the result of corneal and internal ocular aberrations.

The OPD-Scan III instrument software automatically calculates internal eye aberrations from whole eye aberrometry and corneal topography data based on the assumption that the cornea contributes 75% toward the total refractive power of the eye and the crystalline lens 25%. One measurement from each eye was evaluated using software that follows the standards for calculating and reporting the optical aberrations of eyes. For each participant, the seat height was adjusted, and their head and chin were placed properly. The device was realigned before each imaging and this was repeated in case of map incompleteness or blinking error. The measurements were taken across a naturally dilated pupil (mesopic pupil) and we obtained the Zernike coefficients for the total ocular aberrations. Where appropriate, internal and corneal aberrations were exported in the corresponding Zernike coefficients, and total, internal and corneal aberrations were scaled to 5, 4.5, and 4 mm using the expression of Diaz et al. (2009). Higher-order aberrations were measured out to the eighth Zernike order. The parameters analyzed included 1) RMS from third to eight orders of total higher-order aberrations (HOA); 2) RMS of the total spherical aberration (SA); 3) RMS of total coma (CA); 4) RMS of total trefoil (TA); and 5) RMS of total astigmatism (AA).

Subjective questionnaires (SSS and NASA-TLX)

The Stanford Sleepiness (SSS) is a 7-point Likert scale used to evaluate the individuals self-reported activation, which ranges from 1 “very active, alert or awake” to 7 “very sleepy” (Hoddes et al., 1972). The SSS was filled upon arrival to the lab in both experimental sessions. Meanwhile, assessment of mental workload with the NASA-TLX scale was carried out after cognitive tasks. The NASA-TLX is composed of six subscales: Mental demand (How much mental and perceptual activity was required?), Physical demand (How much physical activity was required?), Temporal demand (How much time pressure did you feel due to the rate of pace at which the tasks or task elements occurred?), Performance (How successful do you think you were in accomplishing the goals of the task set by the experimenter?), Effort (How hard did you have to work to accomplish your level of performance?), and Frustration level (How insecure, discouraged, irritated, stressed and annoyed versus secure, gratified, content, relaxed and complacent did you feel during the task? The participants had to score each subscale into 20 equal intervals anchored by a bipolar descriptor (e.g., Low/High), this score was multiplied by 5, resulting in a final score between 0 and 100 (Hart & Staveland, 1988).

Cognitive performance calculation

Regardless of the task (3-back or oddball) each response qualified as a hit (correct click), a false alarm (or commission error, incorrect click), a correct rejection (correctly non-clicking), or a miss (omission error, incorrectly non-clicking). We calculated the hit rate h (correct button pressings /total number of go trials) and the false alarm rate f (incorrect button pressings/total number of no-go trials) for each block of the task (namely, the total number of intervals was divided in 3 equal blocks of 5 intervals (15 intervals in total), and h and f were computed for each of these three block) to check the cognitive performance. Larger h and smaller f values indicate better response discriminability between go and no-go trials. A composite measure of discriminability can be computed as the arcsine of f minus the arcsine of h . The larger this difference of arcsines, the better is the performance in the task (Perales et al., 2005).

Experimental design and statistical analysis

A within-participant repeated-measures design was used to assess the effect of mental task complexity on ocular aberrations. The measurement moment (pre, block 1, block 2 and recovery) and mental workload task complexity (3-back, oddball) were the within-subjects factors, and HOA, SA, CA, TA, and AA RMSs were the dependent variables. We also analyzed the pupil diameters and the heart rate variability at the same points of ocular aberrations with control purposes (see supplementary material), and obtained participant's subjective mental workload via standardized questionnaires and cognitive performance scores.

A T-test for related samples considering mental workload task complexity (3-back, oddball) as the within-subjects factor was carried out to analyze the effect of task complexity on cognitive performance and perceived mental load (NASA-TLX).

Finally, we analyzed total aberrations in mesopic conditions for the RMS of HOA, SA, CA, TA and AA. Then, for those total RMSs in mesopic conditions which showed statistical significance ($p < .05$), we also evaluated corneal and internal aberrations, and pupil diameters were scaled to 5, 4.5, and 4 millimetres. A repeated measures ANOVA were performed using the measurement moment (4) and the mental task level (2) as the within-participants factors for each pupil diameter (mesopic, 5 mm, 4.5 mm, and 4 mm) and type of aberrations (total, internal and corneal).

Results

Cognitive manipulation check

Cognitive performance showed a significant difference between mental task levels [$t(11)=7.466$, $p < .01$]. The high load version (3-back) clearly displayed lower discriminability values than the low version (0.674 ± 0.02 , and 1.49 ± 0.074 , respectively). Still, inspection of confidence intervals (average ± 2.7 standard errors), clearly shows that performance in the 3-back task was much above 0 (the level that would indicate random performance). Also, to examine the effectiveness of mental level manipulation, we tested the subjective mental load reported in each experimental session with the NASA-TLX scale. The subjective result demonstrated higher mental demand in the 3-back task (38.681 ± 3.819) than in the oddball condition (15.069 ± 1.784) [$t(11)=-7.663$, $p < .01$].

Effect of mental task complexity on ocular aberrations

High order RMS

Firstly, total HO RMS with natural pupils yielded no statistical significance for the mental task, the measurement moment and the interaction [$F(1,11)=2.052$, $MSE=.036$, $p=0.18$; $F(3,33)=1.004$, $MSE=.009$, $p=.403$; and $F(3,33)=2.531$, $MSE=.006$, $p=.103$, respectively].

Spherical RMS

Total spherical RMS with natural pupil size displayed no significant differences for the mental task, and neither for measurement moment or the interaction [$F(1,11)=1.104$, $MSE=.013$, $p=.316$; $F(3,33)=.822$, $MSE=.006$, $p=.471$; and $F(3,33)=.191$, $MSE=.002$, $p=.844$, respectively].

Coma RMS

For its part, total coma RMS exhibited no statistical differences for the mental task, measurement moment, and the interaction [$F < 1$ in the three analysis].

Trefoil RMS

Considering natural pupils, the total trefoil RMS showed no statistical significance for the mental task, the measurement moment and the interaction, [$F(1,11)=2.374$, $MSE=.048$, $p=.152$; $F(3,33)=2.106$, $MSE=.015$, $p=0.118$; and $F(3,33)=2.774$, $MSE=.009$, $p=.059$, respectively].

Astigmatism RMS

Firstly, total astigmatism RMS with natural pupils presented signification for the mental task and for the interaction [F(1,11)=7.448, MSE=.004, p=.02, η_p^2 =.701; and F(3,33)=3.171, MSE=.001, p=.037, η_p^2 =.681, respectively] whereas no effect was found for the measurement moment [F<1]. Due to the interactive effect, two separate ANOVAs showed that the 3-back task revealed a marginal significant effect in total astigmatism RMS whereas the oddball condition revealed no statistical significance [F(3,33)=2.392; MSE=.002, p=.086, η_p^2 =.546 versus F(3,33)=.762, MSE=.002, p .487]. Internal astigmatism RMS yielded a significant effect for the mental workload task [F(1,11)=4.332, MSE=.062, p=.049, η_p^2 =.476] and no effect for the measurement moment or the interaction [F(3,33)=1.584, MSE=.055, p=.223; and F(3,33)=1.796, MSE=.042, p=.167, respectively]. In the same line, corneal astigmatism RMS showed signification for the mental task [F(1,11)=4.894, MSE=.067, p=.045, η_p^2 =.523] and again, no effect for the measurement moment or the interaction [F(3,33)=1.516, MSE=.089, p=.239; and F(3,33)=2.248, MSE=.088, p=.101, respectively] (see **Figure 15**).

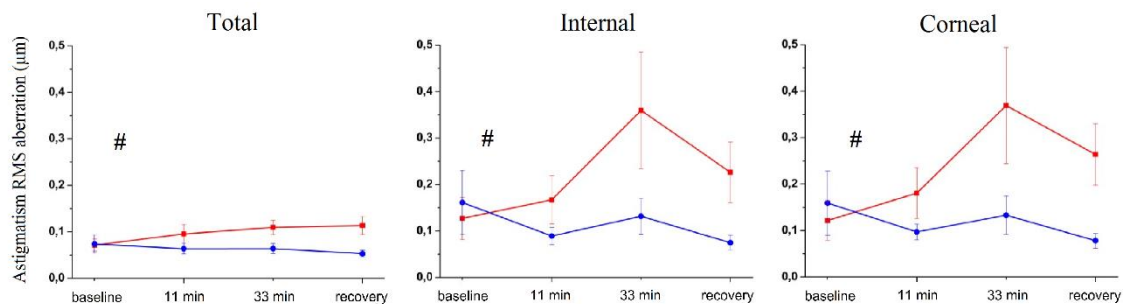


Figure 15. Effects of mental task complexity on astigmatism RMS for total, internal and corneal aberrations with natural pupils. Data from the 3-back condition represented in red, and from the oddball task, in blue. The x-axis shows the four measurement moments, with the measurement before mental workload, the measurements after 11 minutes and 33 min of mental workload, and the recovery measurement (10 min). # indicates statistical differences between task-complexity levels (p-value < .05). Error bars represent the standard error (SE). All values are calculated across participants (n=12).

Secondly, we calculated astigmatism RMS for 5 mm pupil. Total astigmatism RMS yielded effect for the mental task and the measurement moment [F(1,11)=5.016, MSE<.001, p=.047, η_p^2 =.533; F(3,33)=5.154, MSE<.001, p=.005, η_p^2 =.889, respectively] whereas no effect for the interaction [F<1]. Subsequently, the high mental workload condition (3-back) promoted an increasing in total astigmatism RMS [F(3,33)=3.359, MSE<.001, p=.03, η_p^2 =.709] against no changes for the oddball task [F(3,33)=1.16, MSE<.001, p=.34]. Then, internal astigmatism RMS showed no effect for mental task, measurement moment or the interaction of both factors [F(1,11)=2.009, MSE=.001, p=.184; F(3,33)=1.608, MSE=.003, p=.217; and F(3,33)=1.989, MSE=.002, p=.151, respectively]. And corneal astigmatism RMS also showed no effect for any factor (mental task

and measurement moment) or the interaction [$F(1,11)=1.524$, $MSE=.002$, $p=.243$; $F(3,33)=1.366$, $MSE=.003$, $p=.274$; and $F(3,33)=1.202$, $MSE=.003$, $p=.323$, respectively].

When pupils were scaled to 4.5, total astigmatism RMS showed effect for the measurement moment and a marginal effect for the mental task [$F(3,33)=4.455$, $MSE<.001$, $p=.01$, $\eta_p^2=.836$; and $F(1,11)=3.777$, $MSE<.001$, $p=.078$, $\eta_p^2=.426$, respectively] but no effect for the interaction [$F(3,33)=1.589$, $MSE<.001$, $p=.22$]. Separate analysis for each condition showed a significant effect for the 3-back condition, whereas no effect was obtained for the oddball task [$F(3,33)=3.44$, $MSE<.001$, $p=.028$, $\eta_p^2=.716$; and $F(3,33)=1.089$, $MSE<.001$, $p=.366$, respectively]. For its part, internal astigmatism RMS yielded no effect for the two main factors [$F<1$, for both] and for the interaction [$F(3,33)=1.817$, $MSE=.001$, $p=.171$]. And corneal astigmatism RMS also showed no effect for mental task, measurement moment and interaction [$F(1,11)=1.076$, $MSE=.001$, $p=.322$; $F(3,33)=1.001$, $MSE=.001$, $p=.389$; and $F(3,33)=1.329$, $MSE=.001$, $p=.282$, respectively].

Finally, total, internal and corneal astigmatism RMS were calculated for 4 mm pupils. Total astigmatism RMS demonstrated no effect for mental task and measurement moment [$F(1,11)=2.211$, $MSE<.001$, $p=.165$; and $F(3,33)=1.757$, $MSE<.001$, $p=.175$, respectively] and also no effect for the interaction [$F<1$]. No effect was found for both conditions when they were separately analyzed [$F(3,33)=1.406$, $MSE<.001$, $p=.264$ for low-load condition; and $F(3,33)< 1$ for the high-load task]. Similarly, internal astigmatism RMS showed no effect for any factor (mental task and measurement moment) and neither for the interaction [$F(1,11)=1.404$, $MSE=.004$, $p=.261$; $F(3,33)=0.702$, $MSE=.008$, $p=.448$; and $F(3,33)=2.401$, $MSE=.005$, $p=.125$, respectively]. Corneal astigmatism RMS also displayed no effect for any of the two main factors and the interaction [$F(1,11)=1.503$, $MSE=.005$, $p=.246$ for mental task; $F(3,33)=0.959$, $MSE=.007$, $p=.366$ for the measurement moment; and $F(3,33)=2.11$, $MSE=.006$, $p=.158$ for the interaction]. All the astigmatism RMSs with scaled pupils are displayed in **Figure 16**.

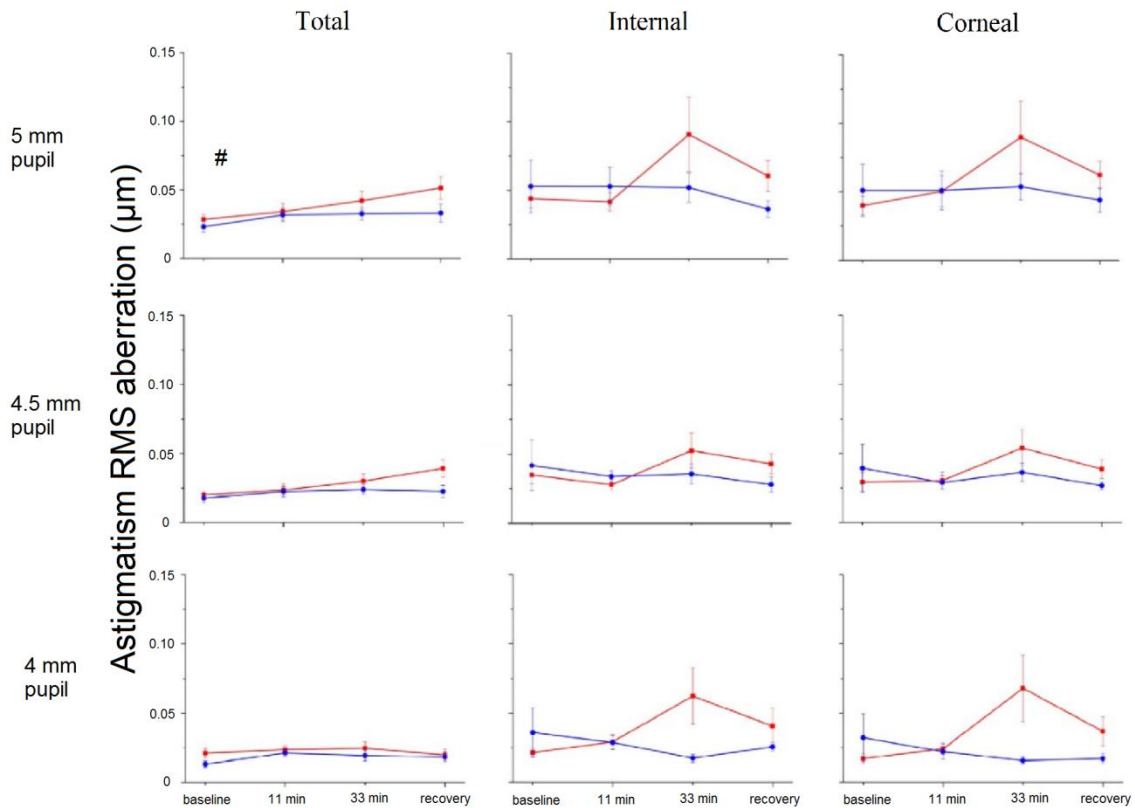


Figure 16. Effects of mental task complexity on astigmatism RMS for total, internal and corneal aberrations with 5, 4.5, and 4 mm scaled pupils. The top, middle and bottom rows represent astigmatism RMS in 5, 4.5 and 4 mm scaled pupils, respectively. The left, middle and right columns represent total, internal and corneal astigmatism RMS aberrations, respectively. Data from the 3-back condition represented in red, and from the oddball task, in blue. The x-axis shows the four measurement moments, with the measurement before mental workload, the measurements after 11 minutes and 33 min of mental workload, and the recovery measurement (10 min). # indicates statistical differences between task-complexity levels (p-value < .05). Error bars represent the standard error (SE). All values are calculated across participants (n=12).

Discussion

In this study, we investigated the effect of mental task complexity on quality optical in terms of higher order aberrations RMSs. Participants performed two cognitive tasks in different days and counterbalanced manner. One task was designed to produce a moderate/high level of working memory load (3-back), whereas the other one was a perceptually matched oddball version. In mesopic conditions, total ocular HOA, SA, CA, and TA RMSs showed no significance differences with respect to task complexity. However, significant changes were presented in AA RMS, showing that higher mental workload complexity (3-back task) promoted an impairment on optical quality. Maintaining a similar behaviour when we scaled to 5, but this effect was missed with 4.5 and 4 mm pupils.

A successful mental task complexity manipulation was corroborated with the cognitive performance score and subjective response (NASA-TLX), showing significant differences in both measures, which indirectly prove that the 3-back task was more difficult than the oddball condition (Cárdenas et al., 2013; Karavidas et al., 2010; Luque-Casado et al., 2015). In addition, we have used pupil size, a classical physiological indicator of cognitive demand-effort, as an autonomous control indices (see supplementary material in appendix) (Wang & Munoz, 2015). Our results showed that pupil size is modulated by cognitive process, greater pupil size in high level of workload and subsiding the pupil size quickly once processing is terminated, being this in agreement with numerous authors (Hess & Polt, 1964; Klingner et al., 2011; Wang & Munoz, 2015). Due to the close relationship between pupil size and ocular aberrations, which has widely been noted in the literature, higher aberrations with larger pupils are expected (Applegate, Donnelly, Marsack, Koenig, & Pesudovs, 2007; Wang et al., 2003). We have scaled to different pupil sizes in order to avoid the pupillary dependence, with the purpose of searching for new ocular indices sensitive to cognitive processing, as we will argue later on.

Total ocular HOA, SA, CA, and TA RMSs showed no changes with the increase of mental task complexity with natural pupils. We only found this effect on AA RMS, increasing the amount of total ocular aberrations with higher mental workload complexity. This variation was also observed for internal and corneal astigmatism RMSs, demonstrating a dual effect from both. When pupils were scaled to 5 mm, a similar behavior was only found for total aberrations. However, with 4.5 and 4 mm pupils no effect of mental task complexity was displayed. Our results are in accordance with Liang (1997), who stated that astigmatism aberrations play a substantial role on retinal image quality when pupil is large but this effect is insignificant with small pupils. The shift from low to high mental workload may be revealed by changes in activity of the autonomous nervous system (ANS) (Miyake et al., 2009; Trimmel et al., 2009), which modulate ocular physiological parameters such as pupil size, ocular accommodation, and intraocular pressure, being those factors tightly linked to ocular aberrations.

Ocular accommodation mainly depends on the accommodative demand stimuli and also it has been established that autonomic variations due to cognitive processing can play an additional role in the variation of accommodative response (Davies et al., 2005; Vera et al., 2016). Corneal and lens changes occur during accommodation, which could affect the aberration pattern. The change in corneal shape and curvature shows contradictory results (Buehren, Collins, Loughridge, Carney, & Iskander, 2003; Pierścione, Popiołek-Masajada, & Kasprzak, 2001; Yasuda, Yamaguchi, & Ohkoshi, 2003), and despite these possible changes, it seems that the modification of corneal HOA aberration is relatively small (He, Gwiazda, Thorn, & Held, 2003). On the other hand, variations in lower order aberrations (defocus and astigmatism) (Mutti, Enlow, & Mitchell, 2001), and in higher order aberrations (Atchison, Collins, Wildsoet, Christensen, & Waterworth,

1995; Cheng et al., 2004; Ninomiya et al., 2002) mainly occur because the shape, position, and refractive index gradient of the crystalline lens modifies (Garner & Yap, 1997; Koretz, Cook, & Kaufman, 2002). However, several authors have indicated that high accommodative levels (greater than 3 D) are necessary to induce significant changes on the RMS of the total higher order (Atchison et al., 1995; Ninomiya et al., 2002) and spherical aberrations (Cheng et al., 2004). In the present study, the stimulus distance is maintained constant with a small accommodative demand (0.4 D) during the entire experiment. Thus the possible changes that may occur in these aberrations could be explained by accommodation dynamic changes due to cognitive processing. However, in our study we have not found significant changes in HOA and spherical RMS aberrations respect to level of mental workload.

Rosales et al. (2008) have shown, in rhesus monkey, that while accommodating a significant tilt or vertical shift of the crystalline lens around the horizontal axis occurs, and it seems feasible that it can be extrapolated in human eyes, with resulting changes in coma and astigmatism aberrations (Cheng et al., 2004). Respect to the coma aberration, the direction and magnitude of the change varies greatly between subjects and no clear trends have been observed during accommodation (Atchison et al., 1995; He, Burns, & Marcos, 2000), so that this aberration would not be an appropriate candidate to capture the effect of mental workload (Atchison et al., 1995; He et al., 2000). In the present study, coma aberration did not show significant changes between tasks. The only ocular aberration that resulted to be sensitive to mental task complexity manipulation was ocular astigmatism aberration even when the pupil size was scaled up to 5 mm. Small pupils diminish the amount of astigmatism aberrations (Liang & Williams, 1997), and similar to our case, we found that scaling pupils under 4.5mm masked the possible effect of mental workload level in this parameter.

Other factor that could influence on ocular aberrations is intraocular pressure, which has been proved to fluctuate during cognitive processes (Brody et al., 1999; Vera et al., 2016). In this regard, Mierdel et al. (2004) reported an association between several Zernike coefficients and changes of intraocular. In the same line, IOP has not been only associated with symmetrical aberrations, but also with asymmetric aberrations, indicating some effect of ocular dynamics on the pattern of aberrations (Asejczyk-Widlicka & Pierscionek, 2007; Qu et al., 2007). We consider that the possible intraocular pressure variations could have an effect on the astigmatism aberrations changes found in this work.

Numerous indices have been investigated to objectively evaluate the level of mental workload (Di Stasi, Antolí & Cañas 2011, Paas et al. 2003). The pupil response is considered one of the most valid and reliable ocular biomarkers to assess mental workload (De Gee, Knapen & Donner 2014, Klingner, Tversky & Hanrahan 2011, Wang & Munoz 2015), but it depends on the illumination levels, presenting practical caveats in ecological settings out of the well-controlled

laboratory conditions. Therefore, other studies have recently focused their attention to find accurate ocular indices sensitive to cognitive load such as accommodative response (Davies et al., 2005; Vera et al., 2016), intraocular pressure (Brody et al., 1999) and saccadic movements (Di Stasi, Antolí & Cañas 2011). Interestingly, this investigation incorporates a promising ocular candidate, astigmatism aberration with scaled pupils up to 5 mm, to assess mental workload that is not dependent of the surrounding illuminations. Although the lapses between mental task performing and aberrations measures are minimal, the lack of monitoring the ocular aberrations measures during the experimental session may be a limitation to our results. In addition, we consider interesting to refute our results with larger sample size, and deepen in other RMSs aberrations such as trefoil aberration to assess mental workload, due to the marginal significance revealed in this study.

In summary, we have shown that mental workload execution modulates astigmatism aberration. These findings may open up a new possibilities concerning the use of astigmatism aberrations as an indicator of mental workload level. It is our hope that future studies probe this index in complex and ecological real settings, and contribute to control the impact of mental workload in applied situations (e.g. driving, flight operations, surgical procedures).

Supplementary material

The effect of mental task complexity on pupil size response

Pupil size (PS) were obtained at the same measurement moments that ocular aberrations, using the OPD Scan III (Nidek Inc., Tokyo, Japan). The same protocol used to measure ocular aberrations was carried out for PS assessment (see Ocular aberrations section for more details).

Mental task complexity manipulation produced significant differences for PS. *Mental task* showed a significant effect [$F(1,11)=4.859$, $MSE=.364$, $p=.048$, $\eta_p^2=.524$], whereas the *measurement moment* and the *interaction* displayed no signification [$F(3,33)=2.47$, $MSE=.058$, $p=.079$, $\eta_p^2=.561$; and $F(3,33)=2.262$, $MSE=.098$, $p=.1$, $\eta_p^2=.521$, respectively]. Two separate ANOVAs for each mental task showed that the 3 back task promoted a significant increase for PS [$F(3,33)=4.047$, $MSE=.065$, $p=.015$, $\eta_p^2=.795$] whereas the oddball condition did not induce any significant change [$F(3,33)=1.106$, $MSE=.098$, $p=.358$] (see **Figure 17**).

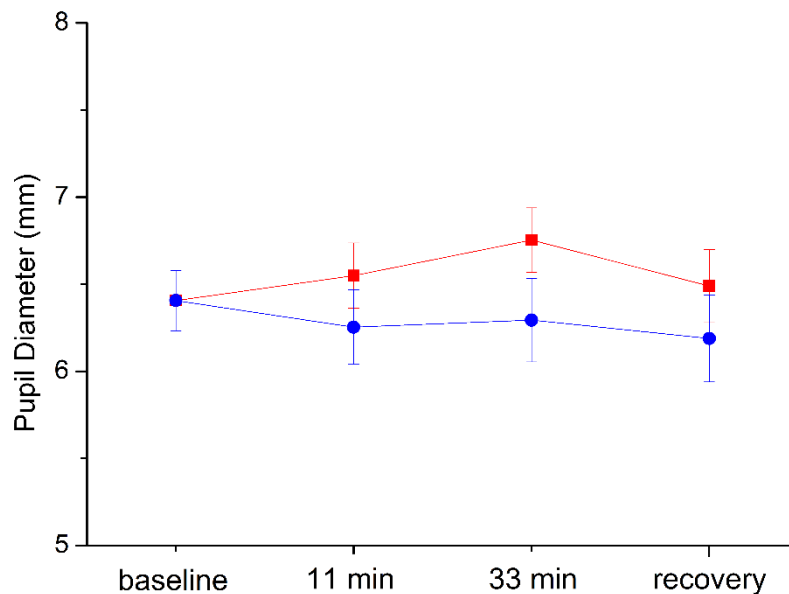


Figure 17. The effect of mental task complexity on pupil size (PS). Mean value for each measurement moment for the 3-back condition (red) and for the oddball condition (blue) (left y-axis). Errors bars represent the Standard Error Mean across participants (n=12).

CHAPTER V: SIMULTANEOUS PHYSICAL AND MENTAL EFFORT

Study 7. Intraocular pressure responses to simultaneous physical/mental effort and predicts subjective sensitivity to physical exertion

Introduction

The interest in the interaction between physical and mental tasks has grown rapidly in recent years, along with the acknowledgement that demands in many situations (e.g. occupational settings, military operations, team sport games) are multiple. In response to this, a number of recent studies have reviewed the influence of physical workload on cognitive performance (Lambourne & Tomporowski, 2010), as well as the effects of mental effort and mental fatigue on physical performance and subjective correlates of physical exertion (Marcora, Staiano, & Manning, 2009).

Demanding physical and mental tasks generate a number of physiological changes, some of which are overlapping (Boksem & Tops, 2008). Cardiorespiratory, musculoenergetic, and hormonal parameters have been demonstrated to be useful indicators of these overlapping processes (Loprinzi et al., 2013), and changes in central nervous system (CNS) activity have also been shown to be significant. For example, Fontes et al., (2013) have recently used functional Magnetic Resonance Imaging (fMRI) to identify brain areas in which activation correlates with increasing degrees of effort in dynamic whole-body exercise.

In view of these effects, and the fact that ocular functioning is closely linked to neurocognitive processes, researchers have focused their attention on ocular variables as potential objective biomarkers of cognitive and physical processes. In this area, micro-saccadic dynamics have been extensively used to assess cognitive impairments (Di Stasi, Catena, et al., 2013), and pupil size has long been known to be very sensitive to manipulations of cognitive and physiological arousal (Wang & Munoz, 2015), and the sensory sensitivity in the visual pathway has been used as an index of physical effort (Zwierko, Lubiński, Lubkowska, Niechwiej-Szwedo, & Czepita, 2011).

The neural mechanisms of these effects have been subject to thorough scrutiny with fMRI in recent studies (Murphy, O'Connell, O'Sullivan, Robertson, & Balsters, 2014).

Intraocular pressure (IOP) has received less attention, and has been studied mostly because of its importance in the management of glaucoma patients (Brody et al., 1999; Rüfer et al., 2014). In healthy individuals IOP correlates with systemic blood pressure during isometric activities (Ashkenazi, Melamed, & Blumenthal, 1992) and depends on factors like fitness level, gender, exercise intensity and duration (McMonnies, 2016; Rüfer et al., 2014) and hydration level during and after exercise (Hunt, Feigl, & Stewart, 2012). Interestingly, the effect of cognitive stressors (e.g. mental arithmetic tasks) on IOP has been much less documented (Brody et al., 1999; Vera et al., 2016), and to date we have not found any work that jointly study the effect of physical exercise and mental load on intraocular pressure. In the present study we test IOP changes after a bout of moderate continuous exercise and check whether this potential effect is modulated by the concomitant presence of different levels of cognitive demands (i.e. working memory load). Also, at the same time we try to determine whether IOP, as measured before exercise, can predict the impact of physical exercise, with concomitant cognitive demands, in subjective assessments of effort intensity and affective valuation of such an effort. In this way, IOP could offer some promise as one of the indices used to evaluate or predict the effect of dual-tasking. We hypothesized that concomitant physical and mental effort can exert a change on IOP, and a possible different variation depending on the mental workload task. We also expected that IOP can estimate subjective perceived exertion, since aerobic exercise involvement is related to lowering intraocular pressure effect.

Our first objective would add to the previously mentioned body of evidence regarding the mechanisms underlying the interaction between cognitive and physical demands. The second one could have profound theoretical and practical consequences for attempts to tailor exercise prescription. More specifically, it is now widely acknowledged that ratings of perceived exertion and subjective affect (degrees of enjoyment vs distress) generated by physical activity not only modulate performance in the ongoing task, but also determine in part the implementation of intentions to be physically active in the future (Ekkekakis, Parfitt, & Petruzzello, 2011). In turn, subtle individual differences (e.g. mood, fitness level, pain tolerance) can modulate these subjective responses to physical activity (Rose & Parfitt, 2007). Among ocular indices, the uniqueness of IOP in reflecting both systemic (i.e. cardiovascular) and neurocognitive processes make it a plausible candidate to capture at least part of such individual differences.

Participants in the present study performed two dual (physical-cognitive) tasks (on different days), matched in physical demands (cycling for 60 min in a cycloergometer, at $60\% \pm 5\%$ of

individually computed reserve heart-rate capacity) but with different cognitive demands. One task was designed to produce a moderate/high level of working memory load (2-back), whereas the other one was a perceptually matched version of the task that did not load working memory (oddball). Ratings of perceived exertion (RPE), basic affect (SAM scale), subjective mental workload (NASA-TLX), and cognitive performance measures were taken during the task, whereas IOP measures were taken before, after 2 min of active recovery, and after 15 min of passive recovery.

Methods

Participants

We conducted the study in conformity with the Code of Ethics of the World Medical Association (Declaration of Helsinki), and permission was provided by the University Institutional Review Board. Eighteen male Sport Sciences students [mean \pm SD, age: 23.28 ± 2.37 yrs (range: 20 to 29 yrs); body mass index: 22.87 ± 1.73 kg/m²; peak power output/Kg: 4.04 ± 0.45 w/kg] took part in the experiment. Admission criteria included (a) being healthy (not suffering any current illness or mental disorder, as assessed by a physician), (b) not presenting any ocular pathology, or any sign of deteriorated visual function (according to the recommendations for clinical management of binocular vision given by Scheiman & Wick, (2008) (c) presenting static monocular visual acuity ≤ 0.0 log MAR in both eyes with the best correction, (d) not taking any medication, and (e) taking regular exercise (at least 3 sessions of moderate exercise per week). We excluded one participant because his RPE responses were inconsistent (he reported maximal exertion values during 40 min). Thus, we analyzed data from seventeen participants (all male, mean \pm SD age: 23.08 ± 2.44 , body mass index: 22.71 ± 1.65 , peak power output/Kg 4.04 ± 0.47). The sample size considered in the present study was based on similar investigations, where statistically significant differences in intraocular pressure during exercise were found (Price, Gray, Humphries, Zweig, & Button, 2003; Rüfer et al., 2014).

According to standard guidelines, participants were classified as belonging to performance level 2. This classification represents performance level from 1 to 5, representing untrained, recreationally trained, trained, well-trained, and professional, respectively, and therefore, the population tested on this investigation fits into the recreationally trained group based on the relative peak power output (De Pauw et al., 2013). All of them were instructed to avoid alcohol consumption and vigorous exercise in the 24 h before any of the sessions, to sleep for at least 7h, not to consume caffeine beverages or other stimulants in the 3h previous to testing, and to follow

a regular diet but avoid eating in the 2h previous to testing. Participants completed the Conlon Survey visual fatigue questionnaire (Conlon et al., 1999) Mean value \pm SD for subjective visual fatigue in our sample was 6.3 ± 0.98 , and all participants scored below 25 (i.e. all scored within the low discomfort range) (Conlon et al., 1999).

Procedure

Participants took part in four sessions. Prior to the first session, we informed the participants about the experimental aims and conditions, and they signed an informed consent form. Subsequently, the visual system of each participant was assessed to check for the inclusion criteria. In this same session, the participants were given instructions and practice with the cognitive task, the RPE, the SAM, and the NASA-TLX scales, so that all athletes were familiar with them before the commencement of the study. After verbal explanation, participants were given five minutes to practice with both mental workload tasks (2-back and oddball).

The second session consisted of the incremental maximal effort test to establish maximum HR, as described above. The session was conducted in the presence of a medical doctor, and a defibrillation device was also at hand. This session was used for a definitive RPE calibration, any questions about using the scale were answered, and participants were encouraged to focus on an overall perception of effort.

The third and fourth sessions constituted the primary focus of the study in which two dual tasks of the same physical effort were performed but each was accompanied by different working memory loads. These were separated by a minimum of 48 h and a maximum of 96 h and both sessions were scheduled at the same time of the day and carried out in a counterbalanced order.

General visual assessment

An experienced optometrist in clinical practice examined to all the volunteers. Visual acuity, accommodative, binocular and oculomotor function were evaluated. The monocular static visual acuity was obtained using a computerized monitor with Snellen optotype (VistaVision, Torino, Italy) at 5 m distance. To assess visual health, we performed biomicroscopic examination and direct ophthalmoscopy to check the anterior and posterior ocular structures. To test the visual function, an ocular refraction examination was performed in each participant, consisting of an objective refraction with non-cyclopegic retinoscopy while the participant maintained a fixed gaze on a distant non-accommodative target, and finally each participant underwent a full monocular and binocular subjective refraction, using and endpoint criterion of maximum plus consistent with best vision. After ocular refraction to achieve the best correction, the following tests were carried out to check the accommodative and binocular function: 1) the accommodative

response was measured by monocular estimate method (MEM) retinoscopy. This was carried out by briefly interposing (in front of one eye at a time), convergent or divergent lenses until neutralizing the reflex found in the horizontal meridian, while the participant read a test close-up with 20/30 letters. 2) The near point of convergence was evaluated by the push-up technique using an accommodative target. A 20/30 single letter test on the fixation stick was used as the target. The target was moved closer until the participant experienced constant diplopia on the stick. This was considered to be the break point, and we measured the distance from the eye to the stick in centimeters as the measurement of the break point. Then we asked the patient to move the target away from the eye until single vision was achieved (recovery point). 3) Static stereo acuity was performed while each participant wore the polarizing viewer. Static distance stereoacuity was tested using the Stereo D6/D8 (VistaVision, Torino, Italy) at 5 m distance. This test presents a range from a maximum of 300 seconds of arc to a minimum of 10 seconds of arc. and only one line from 5 possible choices has crossed disparity. The participant was asked to identify which line seemed to be at a different distance than the other four. Static near stereo acuity was measured using the Randot Stereotest Circles (Stereo Optical Company, Chicago, Illinois) at 40 cm distance. This multiple-choice series tested fine depth discrimination. Within each of 10 targets were 3 circles. Only 1 of the circles had crossed disparity, which, when seen binocularly, would appear to stand forward from the other two. This test presents a range from a maximum of 400 seconds of arc to a minimum of 20 seconds of arc. The level of stereo acuity was recorded as the last series of targets correctly answered. Normal values for visual function parameters were considered by following the recommendations given by Scheiman & Wick (2008). All participants included in this study achieved normal values, according to these criteria.

Maximal effort test and HR assessment

A cycloergometer (Excalibur Sport, Lode, Groningen, The Netherlands) was used to induce physical effort. Participants started warming up, cycling with no resistance for 5 min before the incremental test began. The first 2 min-long effort level was set as the participant's bodyweight/2 W (e.g. a participant weighting 70 kgs started with 35 W). Effort was incremented in bodyweight/2 W steps after each 2 min interval, and the procedure continued until volitional exhaustion. The peak power output (PPO) at the exhaustion point was recorded, and used to classify participants according to their performance level.

Heart rate was monitored using a Polar RS800CX wrist device (Polar Electro Oy, Kmpele, Finland), set to measure heart rate. Data were transferred to the Polar Protrainer Software. Maximal heart rate, as measured at exhaustion, was later used to calculate reserve heart rate (RHR) in the two experimental sessions.

Submaximal physical effort task

The main part of each of the two experimental sessions consisted of cycling for 60 min while performing the mental workload task (2-back, oddball). The rest of measures (IOP, RPE, SAM and NASA-TLX) were taken during or after this task (see details below).

Before cycling, the participant was asked to lie down in a supine position in a quiet room for 6min and HR after this resting period was established as HR_{min} . HR_{max} as computed in the previous session (maximal effort test; see above), and the two HR_{min} measures were used to calculate the reserve heart rate (RHR) for each individual, and each session. The 60 % of the reserve heart rate is calculated using the Karvonen equation as $[(HR_{max} - HR_{min}) \times 0.6] + HR_{min}$ (Karvonen, Kentala, & Mustala, 1957). The participant was then asked to start cycling at bodyweight/2 w. Resistance was increased in bodyweight/2 W steps per minute until reaching $60\% \pm 5\%$ of RHR and this level of effort was then held constant for 60min. Participants were asked to keep on cycling at a frequency between 50 and 70 rpm during the entire session, and current frequency was continuously shown on the cycloergometer display. When HR was higher than 65% of RHR the resistance was manually decreased in bodyweight/4 W steps per minute until reaching $60\% \pm 5\%$ of RHR again. After 60 min of exercise, participants performed 2 min of active recovery at bodyweight/2 w. Finally, participants were asked to sit for 15 min, which was considered as passive recovery.

Mental workload tasks

The cognitive task corresponding to each experimental condition was run simultaneously to the submaximal physical effort task described above, and started upon reaching the $60\% \pm 5\%$ of RHR.

The mental workload task (60min) was split into several three-block phases. Each block consisted of 105 s of task trials (2-back or oddball), followed by a (mental) rest period in which psychometric measurements were taken. The recesses were 15 seconds long between blocks, and 75 seconds long between phases. The physical task was not interrupted during recesses, but in each long recess between phases, participants were allowed to drink water *ad libitum*. The first 8 phases (24 blocks; 56 min in total) were considered for analysis of psychometric measures (the last phase was incomplete and was thus discarded), Nevertheless, all participants performed 25 complete blocks (one in the last phase), and this was therefore, the total number of blocks considered to check cognitive involvement and performance.

The mental workload task (a 2-digit load version of the N-back task) (Owen et al., 2005) consisted of a series of digits (1, 2, or 3), presented randomly, one at a time and at a rate of one digit every 2500 ms (each digit was presented for 1000 ms, and the inter-stimulus interval was 2000 ms). In

each trial, participants were asked if the digit currently on screen was the same as the one presented 2 positions earlier, and press a button every time a match was observed (participants did nothing if there was no match). This task thus requires keeping the two last digits in working memory (working memory load), comparing every new digit with the earliest of them (checking), incorporating the new item and discarding the earliest one for further comparisons (updating). The task can be manipulated to raise or reduce working memory load, depending on the number of digits the participant must keep in mind (2 in the current version of the task).

The oddball task was designed to be perceptually identical to the 2-back task (Luque-Casado et al., 2015). This condition allowed as to control the potential influence of stimulus setting features (e.g. stimulus duration, inter-stimulus interval, see Luque-Casado et al., 2015). Before the task started, a single digit was presented on screen, and the participant was instructed to press the button every time that digit appeared on screen during that session, and to withhold the response for the other 2 digits. This task imposes little or no working memory load, but uses exactly the same stimuli as the 2-back task, requires vigilance during the whole session, and the same rate of response (on average, one response/3 trials) (Luque-Casado et al., 2015).

Stimuli of the cognitive load task were displayed on a 1920 x 1080 LCD monitor, situated 3 m in front of the participant in order to avoid sustained accommodation (~ 0D), while the participant was cycling. Visual stimuli subtended 8.83 min of arc, which corresponds to 0.11 visual acuity, and were thus clearly visible for any participant of this study. Illuminance of the room was quantified at the corneal plane with an Illuminance meter T-10 (Konica minolta, Inc., Japan), and kept constant during the entire experiment (mean \pm SD; 249.04 \pm 6.47 lux).

Whilst cycling, participants held a clicker on their dominant hand to make the responses required for the cognitive task, and a distinctive sound was used as feedback for each response. Independently of the task (2-back or oddball) each response qualifies as a hit (correct click), a false alarm (or commission error, incorrect click), a correct rejection (correctly non-clicking), or a miss (omission error, incorrectly non-clicking). The number of hits, misses, false alarms and correct rejections in each block of the task were recorded for further performance analyses.

Intraocular pressure (IOP)

IOP measurements were obtained with an Icare Tonometer (Tiolat Oy, INC. Helsinki, Finland). The order of first eye measured (right, left) was randomized. IOP was measured just before the submaximal physical effort task (pre), immediately after active recovery (act-rec) and immediately after passive recovery (pas-rec), in the two experimental sessions. In order to

increase internal validity, the mean of the two baseline IOP measurements, obtained in the two different experimental sessions, was used for correlational statistical analysis (see statistical analysis and results). For the IOP measure, participants were instructed to look at distance while the probe of the tonometer was held at a distance of 4 to 8 mm, and perpendicular to cornea. Six rapidly consecutive measurements were taken against the central cornea and the mean reading displayed digitally in mmHg on the LCD screen. The instrument indicated if differences between measures were acceptable or the SD was too large and a new measurement was recommended, we always obtained values with low SD (ideal measure).

Subjective scales and cognitive performance

Rate of perceived exertion (RPE)

Ratings of perceived exertion (Borg CR10 RPE scale) (Borg, 1998) were collected after warming up; at regular intervals whilst cycling (right after every block of the cognitive task); right after submaximal exercise interruption; after 2min of active recovery, and after 15min of passive recovery during the two experimental sessions. This yielded 28 measurement points in total, for each experimental session. The CR 10 RPE scale allows athletes to subjectively estimate the intensity of the physical effort they are exerting at a certain moment in a numerical scale ranging from 0 (“nothing at all”) to 10 (“extremely strong”).

Self-assessment manikin (SAM)

The Self-Assessment Manikin (SAM) scale was used to record the emotional response elicited by the task. This instrument was applied at the same points as the RPE scale. The SAM is a non-verbal pictorial assessment technique that directly measures pleasure (valence), arousal (activation), and dominance elicited by emotionally laden environmental stimuli. In this study, we only used the pleasure-displeasure dimension. SAM scores range from 1 (represented by the icon of a frowning human figure) to 9 (represented by the icon of a smiling human figure) (Bradley & Lang, 1994). The response is given by choosing one of 5 icons displayed horizontally on a sheet (or the intermediate point between two of them). Each response was coded between 1 and 9.

Subjective mental workload assessment (NASA-TLX)

Assessment of mental workload with the NASA-TLX scale (Hart & Staveland, 1988) was carried out only after active recovery. The NASA-TLX is composed of six subscales: Mental demand (How much mental and perceptual activity was required?), Physical demand (How much physical activity was required?), Temporal demand (How much time pressure did you feel due to the rate or pace at which the tasks or task elements occurred?), Performance (How successful do you think you were in accomplishing the goals of the task set by the experimenter?), Effort (How hard did

you have to work to accomplish your level of performance?), and Frustration level (How insecure, discouraged, irritated, stressed or annoyed versus secure, gratified, content, relaxed or complacent did you feel during the task?). The participants were asked to provide scores for each subscale (ranged from 0 to 100). Scores for each subscale, and a weighted total workload score were obtained following standard instructions.

Cognitive performance calculation

Regardless of the task (2-back or oddball) each response qualified as a hit (correct click), a false alarm (or commission error, incorrect click), a correct rejection (correctly non-clicking), or a miss (omission error, incorrectly non-clicking). To check the involvement and performance in the cognitive task, we computed the number of hits, misses, false alarms, and correct rejections in each block. For this, we calculated the hit rate h (hits/total number of go trials) and the false alarm rate f (false alarms/ total number of no-go trials) for the entire mental task. Participants performed a total number of 25 blocks, and for analysis we divided them into five equal parts (phase), resulting in five phases of 5 blocks each. A composite measure of discriminability is the arcsine of f minus the arcsine of h . The larger difference of arcsines, the better performance in the task (Perales, Catena, Shanks, & González, 2005).

Design and Statistical Analysis

To ensure engagement in the cognitive task, the difference in arcsine measures was submitted to a 5 (phase) x 2 (task: 2-back, oddball) analysis of variance (ANOVA), with the two factors manipulated within-participants. Also, each of the 6 NASA-TLX subscale scores was submitted to a one-way ANOVA (with task: 2-back, oddball, as the only within-participant factor).

To check that physical exertion was matched across sessions, average HR and weighted averaged W/Kg were submitted to a paired two-tailed (task: 2-back, oddball) t-test.

As described above RPE and SAM (valence) scores were collected 28 times during each experimental session (after warming up, right after every block of the cognitive task, right after submaximal exercise interruption, after 2 min of active recovery, and after 15min of passive recovery). So RPEs and SAMs (valence) were analyzed using a 28 (measurement point) x 2 (task: 2-back, oddball) within-participant ANOVA (one ANOVA for RPE and another one for SAM-valence).

IOP measures were collected just before cycling began, right after the 2 min active recovery period, and right after the 15 min passive recovery period. Accordingly, IOP values were analyzed

using an ANOVA, with measure moment (pre, act-rec, pas-rec) and task (2-back, oddball) as within-participant factors. We used the Bonferroni-correction for multiple comparisons.

As noted above, the second aim of this study was to ascertain whether IOP, as an individual difference measure, can predict the impact of physical exercise, with concomitant cognitive demands, on subjective assessments of effort intensity and affective valuation. Accordingly, we performed, first, two ANCOVAs (one for each mental condition) with RPE as a dependent measure, measurement point (1-28) as within-participant factor, and baseline IOP as continuous covariate. Secondly, the same two analyses were carried out with SAM-valence as the dependent measure. Finally, equivalent ANCOVAs were carried out with RPE and SAM as dependent measures, but using the fitness level as covariate for both mental workload task levels, instead of baseline IOP.

Four analyses of covariance (ANCOVA) were carried out for the two tasks and the two subjective estimate variables (RPE and SAM-valence), namely, one ANCOVA for SAM-valence in the mental workload task, a second one for SAM-valence in the oddball task, a third one for RPE in the mental workload task and a fourth one for RPE in the oddball task. In all of them, measurement point (1-28) was a within-participant factor, and IOP and fitness level (peak power output) were continuous covariates. These analyses were carried out to investigate whether RPE and SAM values across measurements in each load task depended on baseline IOP and fitness level.

Finally, linear regression analyses were performed for each measurement moment (28) in each experimental condition (task: 2-back, oddball) for RPEs and SAMs valence using baseline IOP values and fitness levels as independent variables. IOP and fitness level standardized regression coefficients were used as independent indices of covariation, specifically, to visually depict the degree to which IOP determined RPE and SAM during each task, without the potentially confounding role of fitness level (and vice versa).

For all analysis, violations of sphericity were managed by adjusting the degrees of freedom according to the Greenhouse-Geisser method, as implemented in SPSS22 IBM software. An α of .05 was adopted to determine significance.

Results

Cognitive manipulation check

Figure 18 displays the (difference of arcsines) discriminability measure across the constant effort part of the session (divided in 5 equal-length phases), for the mental workload (2-back) and the

oddball versions of the task. The one-way ANOVA showed a significant effect of the cognitive task [$F(1,16) = 79.934$, $MSE = 0.077$, $p < .01$, $\eta_p^2 = 1$]. Neither the effect of measurement point (1-5) nor the task x measurement point interaction were significant [$F < 1$, for both]. As expected, discriminability reflected the different difficulty levels of the two versions of the task, with the mental workload version eliciting lower discriminability values than the oddball version. Still, inspection of confidence intervals (see SE bars in the figure), clearly shows that performance in the mental workload task (2-back) was well above 0 (the level that would indicate random performance), which demonstrated high and virtually constant involvement of participants in the cognitive task during the whole session.

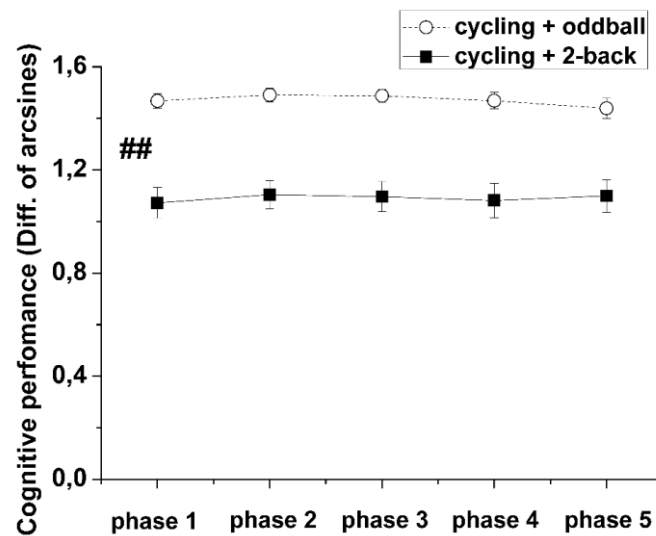


Figure 18. The effect of cognitive task level on discriminability scores. Average discriminability value for each cognitive task level (y-axis). ## indicates significant main effect of cognitive load (p -value < 0.01). Error bars represent the Standard Error (SE) across participants (n=17).

Table 9 shows scores for the six NASA-TLX subscales, along with results of ANOVA tests across tasks. *Mental demand* was judged to be higher in the mental workload task than in the oddball condition. Somewhat surprisingly, however, the oddball condition was judged to be more physically demanding than the mental workload task.

Table 9. NASA-TLX scores across cognitive task level and subscales. Average \pm Standard Deviation, of NASA-TLX subscales for both mental levels, calculated from all participants (n=17). Values range between 0 and 500. Higher scores indicate higher perceived task load. * indicates statistically significant differences between the measuring session, $p < 0.05$.

NASA-TLX Subscale	2-Back task	oddball task	p
Mental demand *	219.71 \pm 134.48	42.06 \pm 81.45	<0.01
Physical demand *	130.59 \pm 88.09	203.82 \pm 110.32	<0.01
Temporal demand	212.35 \pm 129.21	255.29 \pm 120.37	0.201
Performance	95.29 \pm 70.37	105.59 \pm 106.4	0.674
Effort	196.47 \pm 124.31	152.64 \pm 62	0.208
Frustration level	46.47 \pm 104.52	4.11 \pm 9.39	0.104

Physical manipulation check

Exercise intensity was successfully kept within the range RHR 60% \pm 5%. A paired two-tailed t-test across task types on mean HR values was non-significant [average \pm SD: 146.39 \pm 8.75 bpm for the oddball, and 145.03 \pm 9.28 bpm for the mental workload, $t(16) = 1.438$, $p = .17$]. The two sessions did not differ in objective physical output [132.7. \pm 28.44 and 131.53 \pm 28.35 w/kg in the oddball and mental workload tasks, respectively, $t(16) = 0.37$, $p = .716$]. Hence, the cognitive task manipulation across sessions did not affect the objective physical demands of the task.

Effects of physical effort and cognitive task level on RPE and SAM (valence)

For RPE measures, there was a significant effect of measurement point (with increasing RPE values across the 60 min session and decreasing RPE during recovery) [$F(27,432) = 33.956$, $MSE = 1.213$, $p < .01$, $\eta_p^2 = 1$]. Task type and the interactive effect were far from having any effect on RPE [$F < 1$, for both].

SAM-valence scores yielded statistical significance for measurement point and task type (increasing physical exertion and heightened cognitive demand elicited lower valence scores) [$F(27,432) = 10.1$, $MSE=0.812$, $p < .01$, $\eta_p^2=1$ and $F(1,16) = 5.727$, $MSE = 8.558$, $p = .029$, $\eta_p^2 = 0.613$, respectively]. The interactive effect was not significant [$F < 1$].

Effects of physical effort and cognitive task level on IOP

As noted above, there were three measurement points for IOP (one at baseline, one right after active recovery, and a last one after passive recovery). There was a significant effect of measurement point on IOP [$F(2,32) = 7.493$, $MSE = 3.966$, $p < .01$, $\eta_p^2 = 0.919$], but no effects

of task type or task type x measurement point [$F(1,16) = 0.09$, $MSE = 5.314$, $p = .768$, and $F(2,32) = 1.164$, $MSE = 2.534$, $p = .323$, respectively]. Two separate ANOVAs were performed for each cognitive condition, showing a significant effect for the 2-back condition [$F(2,32) = 8.534$, $MSE = 3.364$, $p < .01$, $\eta_p^2=0.951$] but no significance (marginal) was obtained for the oddball condition [$F(2,32) = 2.591$, $MSE = 3.909$, $p = .092$, $\eta_p^2 = 0.474$]. Bonferroni-correction for multiple comparisons showed that simultaneous resistance exercise and mental workload demand (n-back) promotes that IOP increased from baseline to the end of active recovery and to the end of passive recovery (corrected p -values = .026 and .003, respectively), but did not significantly change between the end of active recovery and the end of passive recovery (corrected p -value = 1). In other words, IOP increased after exertion, and 15 minutes of rest were insufficient to generate a significant reduction in the mental workload condition (see **Figure 19**). However, cycling 60 minutes and performing the oddball version of mental workload induced no significant changes on IOP.

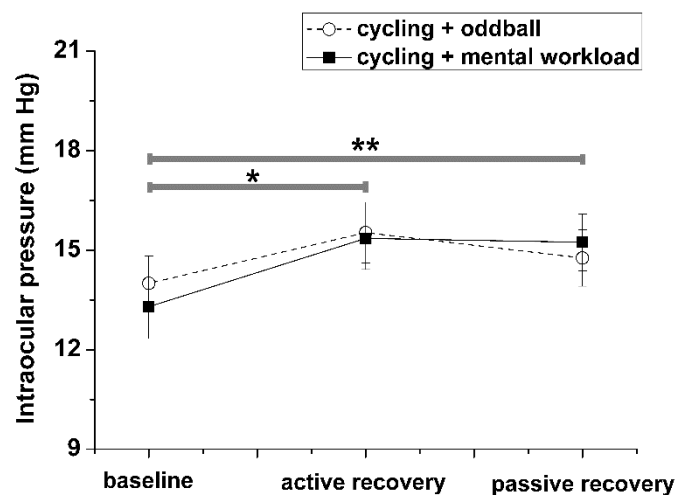


Figure 19. The effects of physical and mental load on intraocular pressure (IOP). Average IOP value for each cognitive task level (y-axis). \$\$ indicates significant main effect of measurement moment (p -value <0.01). ** and * indicate statistically significant differences between the measurement point (corrected p -value <0.01 and <0.05 , respectively). Error bars represent the Standard Error (SE) across participants ($n=17$).

The utility of IOP and fitness levels to predict RPE and SAM valence

The first ANCOVA on RPE in the oddball task yielded a significant effect for measurement moment [$F(27,405) = 2.733$, $MSE = 0.64$, $p < .01$, $\eta_p^2=1$], no significant effect for the interaction measurement moment x IOP baseline value [$F(27,405) = 0.8$, $MSE = 0.64$, $p = .754$], and a significant main effect for the between-participant factor (baseline IOP) [$F(1,15) = 5.901$, $MSE = 12.168$, $p = .028$, $\eta_p^2 = 0.622$]. In the condition with concomitant mental workload (2-back task) the measurement point showed significance [$F(27,405) = 4.497$, $MSE = 0.959$, $p < .01$, $\eta_p^2 = 1$],

but no significant effect was found for the interaction measurement point x IOP baseline value [$F(27,405)=1.223$, $MSE = 0.959$, $p = .164$], or the covariate factor [$F(1,15) = 0.729$ $MSE = 42.281$, $p = .407$].

Secondly, parallel ANCOVAs for SAM valence in each experimental condition using IOP baseline value as the covariance factor were performed. In the oddball task, no effect was found for measurement moment, the interaction, or the between-participants factor (baseline IOP) [$F(27,405) = 0.644$, $MSE = 0.478$, $p = .917$; $F(27,405) = 0.216$, $MSE = 0.478$, $p = 1$; and $F(1,15) = 3.313$, $MSE = 25.214$, $p = .089$, $\eta_p^2=0.399$, respectively]. No effects were found either in the task with concomitant mental workload [$F(27,405) = 1.225$, $MSE = 0.768$, $p = .205$; $F(27,405) = 0.586$, $MSE = 0.768$, $p = .953$; and $F(1,15) = 0.542$, $MSE = 43.95$, $p = .473$, respectively].

Equivalent analyses were carried out with fitness level as the covariance factor, and RPE and SAM (valence) as dependent measures. An ANCOVA for RPE during the oddball condition showed no significant effects for measurement point, the interaction measurement moment x fitness level [$F(27,405) = 1.324$, $MSE = 0.629$, $p = .131$; and $F(27,405)=1.072$ $MSE = 0.629$, $p = .37$, respectively], or fitness level [$F(1,15) = 0.035$, $MSE = 16.915$, $p = .855$]. In the task with concomitant mental workload (2-back task), effects were significant for measurement moment [$F(27,405) = 4.182$, $MSE = 0.825$, $p < .01$, $\eta_p^2=1$] and for the interaction measurement point x fitness level [$F(27,405) = 3.92$, $MSE = 0.825$, $p < .01$, $\eta_p^2 = 1$]. No independent effect was found for the between-participant factor [$F(1,15) = 0.644$, $MSE = 42.511$, $p = .435$].

The analysis of covariance for SAM valence using fitness level as the covariance factor and with the oddball condition yielded no effect for the measurement moment or the interaction measurement moment x fitness level [$F(27,405) = 0.545$, $MSE = 0.474$, $p = .971$; and $F(27,405) = 0.348$, $MSE = 0.474$, $p = .999$, respectively]. A significant effect was observed for the covariance factor [$F(1,15)=4.967$, $MSE = 23.125$, $p = .042$, $\eta_p^2 = 0.55$]. No effects were found in the task with mental workload (2-back task) for measurement moment, the interaction, or the between-participants factor (fitness level) [$F(27,405) = 0.703$, $MSE = 0.773$, $p = .866$; $F(27,405) = 0.49$, $MSE = 0.733$, $p = .986$; and $F(1,15) = 0.375$, $MSE = 44.426$, $p = .549$, respectively].

Finally, we performed linear regression analyses with IOP and fitness levels as predictors for each RPE and valence value in all of the 28 measurements points of the two tasks (112 regression analyses in total). Standardized regression coefficients (β) from these analyses are displayed in **Figure 20**. These coefficients can be interpreted as indices of dependence of valence and RPE on fitness level and IOP, and thus as visual representations of the effects described above. These analyses are also interpretable in their own right, and demonstrate that IOP is consistently

predictive of RPE during the first measurement points of the oddball task and, in a less consistent manner, during the first measurement points of the mental workload task.

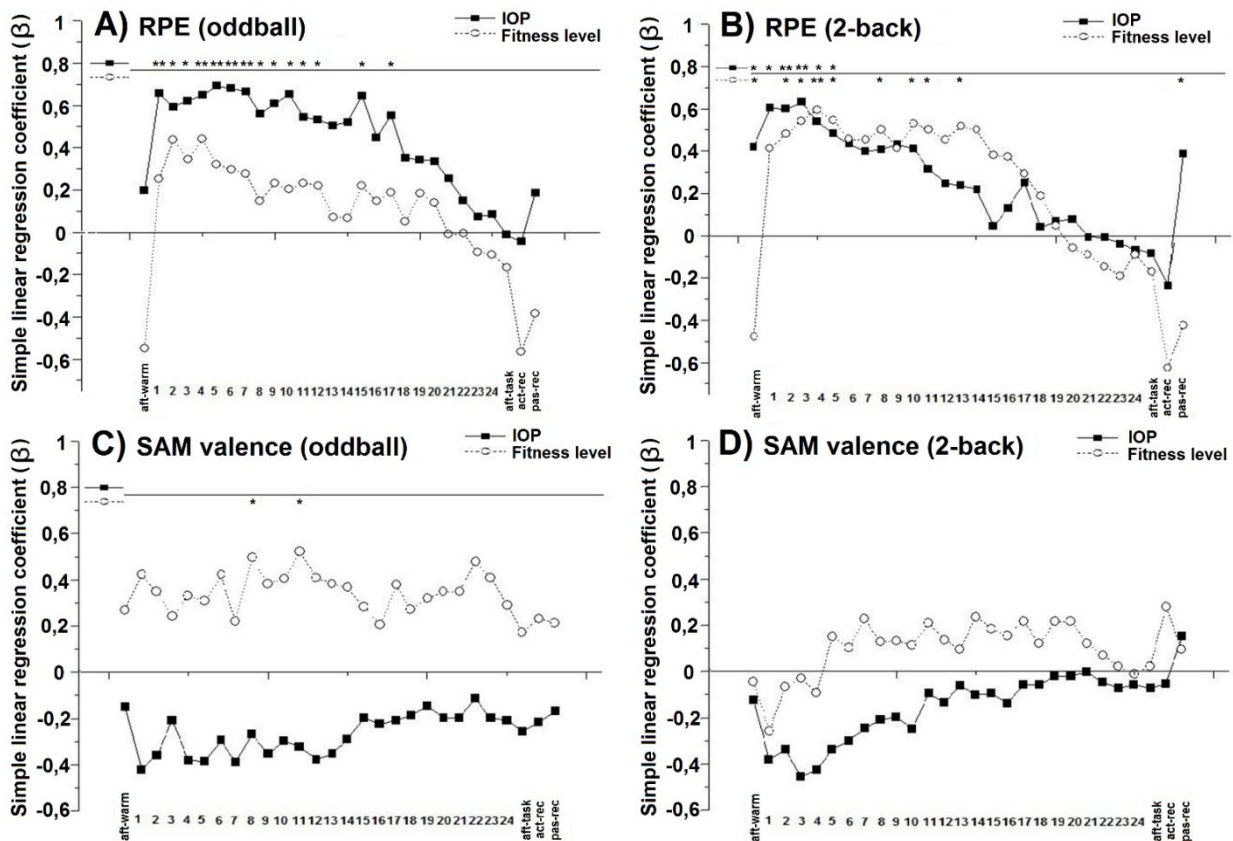


Figure 20. Relationship between IOP and fitness level with RPE and SAM valence for each measurement moment and cognitive load. A) Regression coefficients for each RPE measure in the oddball condition; B) Regression coefficients for each RPE measure in the 2-back condition; C) Regression coefficients for each SAM valence measure in the oddball condition; D) Regression coefficients for each SAM valence measure in the 2-back condition. The x-axis displays the different measurement moments during the experiment. “Aft-warm” indicates the measure after 2 minutes of warming up, from 1 to 24 are represented the subjective scales reported by participants after each mental block, “aft-task” means the measure obtained just after finishing the dual task, “act-rec” corresponds to the measure collected after 2 minutes of active recovery, and lastly, “pas-rec” represents the measure after 15 minutes of passive recovery. ** and * indicate statistically significant differences (p -value < 0.01 and <0.05, respectively). Regression coefficients are calculated across participants ($n=17$).

Discussion

Results show that, as hypothesized, IOP increased after a dual task comprising submaximal exercise and a cognitive task, and had not fully returned to baseline even after a 15 min passive recovery period. This is, by itself, an interesting finding. Showing that two levels of cognitive demand with simultaneous resistance exercise exert different effects on ocular physiology.

In view of our results, the possibility exists that both tasks influenced IOP but more cognitive demanding tasks add an effect on IOP to that presumably expected from just physical exertion or while performing the oddball version simultaneously. In fact, in a recent study we have shown that despite not imposing demands on working memory, the oddball condition does require sustained attention. This is sufficient for the task to induce changes in heart rate variability (HRV), when compared to a number of control conditions (Luque-Casado et al., 2015). We cannot discard the possibility that a similar mechanism could be in operation in the case of IOP.

In spite of this, and although the implications are beyond the aims of the present study, the high-load version of the task elicited lower valence ratings than the low-load task. In other words, working memory load made the dual task significantly less pleasurable. This was accompanied by a lack of effect on RPE and, quite somewhat surprisingly, a contrary effect on ratings of physical demand, as measured by the corresponding subscale of the NASA-TLX scale. This pattern of effects partially contradicts the general idea that cognitive load increases perceived exertion (Marcora et al., 2009). As Cárdenas et al. (2013) suggested, demanding cognitive tasks can redirect the athlete's focus of attention, and thus reduce perception of effort. Distracting effects are the basis of dissociative effort tolerance techniques (Brick, Macintyre, & Campbell, 2014), and could explain why exercising during the oddball task was retrospectively judged as *less* physically demanding (according to the NASA-TLX) than during the mental workload task, yet at the same time exercising during the oddball task was judged as more pleasurable than during the mental workload task. The fact that RPE remains insensitive to the working memory load manipulation could indicate that it is subject to two mutually counteractive effects. This question, and why seemingly overlapping RPE and NASA-TLX subscales do not show exactly the same effects, certainly deserves further investigation.

Regarding to the second aim of the study, IOP partially predicted subjective sensitivity to effort. In the oddball version of the task, RPE ratings reflected a significant effect of IOP. More specifically, people with higher IOPs judged the dual task to be harder in terms of subjective physical effort. Although the IOP x measurement moment did not reach significance, point-by-point regression analyses suggested that the effect of IOP tended to diminish as perceived exertion mounted (as reflected in the fact that IOP-RPE correlations were progressively lower across the task, and fell below significance after approximately the first half of the session). Neither was the IOP effect significant in the 2-back session.

In summary, results strongly suggest that IOP predicts sensitivity to exertion in low demand situations, that is in relatively moderate intensity, short duration physical activities, with less demanding cognitive tasks (at least less demanding in term of working memory load). In practical

terms, this would imply that people with higher IOPs tend to find less enjoyment and perceive more effort in precisely those tasks that seem to be better tolerated by the general population. Moreover, this effect is mostly independent of the individuals' fitness level.

To date, sensitivity to effort had been shown to depend on constitutional variables (mostly BMI and fitness level) (Garcin, Mille-Hamard, & Billat, 2004), on cognitive factors (self-efficacy, expectations) (Noakes, 2012), and also on mood states (Ekkekakis et al., 2011). The influence of these factors, however, is more evident in higher rather than lower physical activity. That is, fitter, slimmer people, when in a better mood, or with higher expectations, tend to tolerate high intensity physical activity better. IOP, however, seems to predict tolerance to less strenuous activities, independently of fitness levels. Hence, the IOP measure seems unique not only because, unlike the previously mentioned factors, it is an ocular-physiological variable, but also because its predictive value is likely to be based on a different mechanism.

A plausible physiological explanation

With regard to our first research question, the level of adrenergic activity plays an important role in the IOP fluctuations. Higher levels of central nervous system activity (e.g. sympathetic innervation) promote aqueous humor production through the ciliary process (Bill, 1975), and also cause pupil dilation (Wang & Munoz, 2015), which reduces the aqueous humor outflow through the trabecular meshwork, the canal of Schlemm, and the collector channels. Thus, higher levels of activation can promote IOP increases, and more interestingly, the concomitant cognitive task causes a slower recovery of IOP as has been demonstrated with perceived exertion (Cárdenas et al., 2013b). Another explanation worthy of consideration is that hydration levels could alter IOP values. As indicated by Hunt et al., (2012) an intraocular pressure reduction occurs when dehydration exists during dynamic exercise, but IOP remains relatively stable when hydration is constantly maintained, as happened in our study. Also, the elevated blood pressure during exercise may enhance the mechanism causing IOP elevation (McMonnies, 2016). Thus, factors such as activation state, hydration levels and blood pressure should all be considered when explaining IOP changes during physical and cognitive tasks. Additionally, aerobic exercise has been demonstrated to decrease IOP after a longitudinal training plan (McMonnies, 2016). Therefore, we can expect that people with better fitness levels show lower baseline IOP values and perceive less exertion during acute resistance exercise. Many questions remain with regard to understanding this mechanism. Beyond the fact that, as with other variables (i.e. HRV), IOP reflects psychophysiological states (e.g. stress) (Yamamoto et al., 2008), there is little basis to speculate about the reasons why it could make people more or less effort-tolerant.

Research limitations

Our study had several limitations. Firstly, this investigation has been conducted with male individuals, while some studies highlight differences in the effect of exercise on intraocular pressure between male and female participants (McMonnies, 2016). Secondly, our hypothesis has been tested during moderate continuous exercise using a cycloergometer for a period of 60 min at $60\% \pm 5\%$ of RHR with concomitant mental demand, and therefore our results can only be viewed against the type of protocol carried out in this investigation and need further investigation with different physical and mental tasks. Thirdly, the level of hydration is important for IOP changes (Hunt et al., 2012) and more studies with water restriction could provide interesting results. Additionally, one of the main conclusions from this study, IOP increases after concomitant physical and mental demands, and therefore the identification of this risk factor associated with undiagnosed glaucoma is of great interest in the prevention and treatment of glaucoma in the community. A future research should include the participations of glaucoma suspects or sufferers (Rüfer et al., 2014) and thus both sports professional and eye health professional could advise the appropriate type of exercise (e.g. about intensity and duration) as well as hydration guidelines during the same that not produce long-term glaucomatous damage (Hunt et al., 2012; McMonnies, 2016; Rüfer et al., 2014). And lastly, the novel application of using IOP as a predictor of effort tolerance has a huge practical implication in sport and offers a new line of research into the field of sport science and exercise physiology. It does, however, require further investigation to clarify its use. Monitoring IOP patterns during sporting activities using the recently developed contact lens sensors would allow more reliable conclusions about the fluctuations of IOP over time to be made (De Smedt et al., 2012).

Conclusions

The present study revealed that intraocular pressure increases after a dual task of moderate continuous exercise (60 min at $60\% \pm 5\%$ of RHR) combined with cognitive demand, and a more demanding task contributed to higher IOP increasing. This investigation also provided the first experimental evidence that intraocular pressure partially predicts subjective perceived effort. This study has two important applications. A broad range of daily activities require both physical and mental demands. Therefore, ophthalmologists and optometrists should consider the acute effect of simultaneous physical and mental effort in those persons with glaucoma or suspected of having glaucoma. Avoiding or reducing IOP fluctuations may improve the prognosis for patients with glaucoma or those at risk of developing it. Secondly, the possible application of IOP as a predictor of effort tolerance offers potentially promising developments in the field of sports physiology and sports psychology.

Study 8. Variations in visual function during a concomitant physical and mental task

Introduction

The visual system is the main channel to gather information by an athlete during sports activity, although the level of expertise, discipline, and position role (in team sports) determine the visual requirements in a game (Memmert, Simons, & Grimme, 2008). It is well known that during the final stages of a match or performance, an athlete's skill often declines, with the deterioration attributed to fatigue (Royal et al., 2006). Meanwhile, conscious and unconscious decision making plays a role in fatigue states and processes (Marino, Gard, & Drinkwater, 2011). Accordingly, sport games require physical and mental effort simultaneously, and athletes experience physical and mental fatigue during sport practice. Therefore, researchers focus their attention on investigating the effect that physical and mental demands exert on athletes' physiology and performance (Cárdenas et al., 2013; Marcora et al., 2009).

Overlapping physical and cognitive requirements generate physiological changes in cardiorespiratory, musculoenergetic, and hormonal indices (Bray et al., 2012; Hillman et al., 2008; Sluiter et al., 2000), and also the central nervous system has been demonstrated to be sensitive to physical and cognitive demands (Leandro L. Di Stasi et al., 2015; Fontes et al., 2013). The eyes originated as outgrowths of the brain and therefore are considered part of the central nervous system (Di Stasi et al., 2012). In view of this relationship, and the fact that ocular functioning can capture physiological changes as the cause of physical and cognitive processes, some investigators are using ocular indices as potential objective biomarkers of physical and mental effort. In this area, pupil size (Hayashi et al., 2010; Wang & Munoz, 2015), saccadic velocity (Di Stasi, Catena, et al., 2013), eyelid dynamics (McIntire, McKinley, Goodyear, & McIntire, 2014), intraocular pressure (Brody et al., 1999; Najmanova et al., 2016; Vera et al., 2016), accommodative response (Davies et al., 2005; Vera et al., 2016), tear osmolality (Ungaro et al., 2015) and critical flicker fusion (Davranche & Pichon, 2005; Luczak & Sobolewski, 2005) have been used to evaluate the effect of physical and/or mental tasks on human physiology. Moreover, ocular indices capture the effect of physical and mental effort, and make the ocular functioning susceptible to being affected by either physical or mental demands.

Previous studies tend to indicate that athletes present better visual skills than do non-athletes, although this issue has not yet been settled (Barrett, 2009). The assumption prevails that abilities involved during each sport are improved due to constant involvement of visual function

(Quevedo-Junyent et al. 2011). Also, there is a belief that visual training improves sport performance (Barrett, 2009; Quevedo & Solé, 1995). However, the influence of physiological stress on visual function due to acute exercise has been scarcely investigated, and present methodological limitations, including the lack of objective physical control and sample characteristics (Myers, 1976; Woods & Thomson, 1995). In addition, related to this perspective, recent studies have reported that peripheral visual perception is impaired during strenuous exercise (Ando, 2013), and Thomson et al. (2009) stated that fatigue can constrain perceptual processing, which is linked to the execution of motor procedures required during ball-game participation. No study to date has jointly analysed the influence of physical and mental load on visual function. In considering the previous results that relate ocular changes to physical and mental effort, we hypothesised that visual function can be altered by homeostatic changes after physical demand, and the simultaneous cognitive resources needed during the task can also add an effect on these changes.

Participants performed two dual (physical-cognitive) tasks (on different days). Both experimental sessions demanded the same physical effort (cycling for 60 min in a cycloergometer, at 60 % \pm 5% of individually computed reserve heart-rate capacity), but the cognitive demands were manipulated using a mental workload task (2-back) and the corresponding oddball task. Visual variables used in clinical practice, such as the near point of convergence (NPC), near stereoacuity, and accommodative facility (Hart Charts) were used to test visual function, and also perceptual-motion capability was investigated by eye-hand coordination. All measures were collected before the task and right after 2 min of active recovery (in counterbalanced order between subjects), whereas the subjective mental workload (NASA-TLX) was measured after 2 min of active recovery at dual-task completion, and cognitive measures were monitored during the entire experimental session (60 min).

The main aim of this study was to assess the effect of physical and mental effort on visual function and eye-hand coordination. In other words, the consequences of exercise-induced fatigue on perceptual and motor processing. A direct application could lead from this study due to possible influence of perceptual impairment in athlete's performance. Nevertheless, the possible influence of visuo-perceptual changes after exercise in consecutive tasks to sport practice (e.g. driving or working) should be considered, as well as the possible association between performing demanding exercise regularly and eye health.

Methods

Participants and ethical approval

A total of 18 male Sport Sciences students at the University of Granada (Spain) [*mean* \pm *SD*, age: 23.28 \pm 2.37 yrs; body mass index: 22.87 \pm 1.73kg/m²; peak power output/Kg: 4.04 \pm 0.45w/kg] took part in this experiment. This study was conducted abiding by the Code of Ethics of the World Medical Association (Declaration of Helsinki) and permission was provided by the university Institutional Review Board (IRB). All volunteers were informed about the experimental aims and conditions, and signed an informed-consent form prior to the study.

Admission criteria included: a) being healthy (not suffering any current illness or mental disorder); b) not presenting any ocular pathology, or any sign of deteriorated visual function (according to the recommendation for clinical management of binocular vision given by Scheiman & Wick 2008; see “General visual assessment for details” c) presenting static monocular (in both eyes) and binocular VA \leq 0 log MAR (\geq 20/20), d) scoring less than 25 on the Conlon Survey (Conlon et al., 1999) and less than 21 at the CISS (Convergence Insufficiency Symptom Survey) (Rouse et al., 2004), d) not taking any medications, and e) taking regular exercise (at least 3 sessions of moderate exercise per week). All participants were instructed to avoid alcohol consumption and vigorous exercise 24 h before any of the sessions, to sleep for at least 7 h, not to consume caffeine beverages or other stimulants in the 3 h prior to testing, and to follow the regular diet but not to eat 2 h before testing.

General visual assessment

Before the experiment started, a board-certified optometrist (JV) examined the visual acuity (VA), accommodative, and binocular function of the participants. Firstly, monocular and binocular VA was determined using a computerized monitor (VistaVision, Torino, Italy) with the logarithmic letters chart test employing the Bailey-Lovie design at a distance of 5m. Then, binocular and accommodative test procedures and normal values for age range were considered following the recommendation of Scheiman & Wick (2008). All optometric tests listed below considered as the inclusion criteria: a) the accommodative response, measured by the monocular estimate method (MEM) retinoscopy, was carried out by very briefly interposing, in front of one eye at a time, convergent or divergent lenses until neutralizing the reflex found in the horizontal meridian, while the participant read a test close-up with 0.18 log MAR (20/30) letters. b) Near and distant horizontal and vertical phoria, evaluated by Thorington’s method. Participants situated at 5 m from the point test (distance horizontal phoria) and 40 cm (near horizontal phoria), held the Maddox bar horizontally in front of their own right eye and were asked to indicate what point of

the horizontal axis of the Maddox cross the red vertical line was situated. Afterwards, the vertical phoria was measured in a similar way, but rotating the Maddox bar vertically, while the volunteer indicated at what point of the vertical axis of the Maddox cross the horizontal line was situated,

c) The near point of convergence, evaluated by the push-up technique using an accommodative target, and this procedure was carried out three times with a 30-s break between measures, considering the average value for analysis. A 0.18 log MAR (20/30) single letter on the fixation stick was used as the target. The target was moved closer until the participant experienced constant diplopia on the stick or the participant objectively lost and regained ocular alignment. This was considered to be the breakpoint, for which we measured the distance from the eye to the stick. This distance expressed in cm constituted the measurement of the breakpoint. Then we asked the patient to move it away from the eye until single vision was restored to establish the recovery point.

d) Near and distance negative and positive vergence amplitude. The negative fusional vergence was measured first to avoid affecting the vergence-recovery value because of excessive stimulation of convergence. A gradually increasing prism bar was introduced for the dominant eye while the patient fixed the gaze on a column of the Snellen optotype, corresponding to the highest visual acuity at 40 cm and 6 m fixation, respectively. When the prism caused double vision in the participant, the amount of prism (breakpoint) was recorded. The prism power was then reduced until the double images could be fused again (recovery point).

e) Static near stereoacuity was measured while each participant wore a polarizing viewer, and using Randot Stereotest Circles (Stereo Optical Company, Chicago, IL, USA) at a distance of 40 cm. This multiple-choice series tested fine depth discrimination. Within each of the 10 targets, there were 3 circles. Only 1 of the circles had crossed disparity, which, when seen binocularly, would appear to stand forward from the other two. This test presents a range from a maximum of 400 seconds of arc to a minimum of 20 seconds of arc. The level of stereo acuity was recorded as the last series of targets correctly answered (Boden et al., 2009).

Finally, f) the accommodative facility using the Hart Chart in binocular viewing condition was assessed. Participants were instructed to read the Hart Chart alternatively one letter at 5 m in primary position and another at 40 cm with the Hart Chart placed 30° inferiorly, both Hart Charts being high contrast (90%). The examiner gave instructions for focusing each letter before each shifting to the next one (starting with the far chart), and the number of cycles completed in 60 s were counted for further analysis.

Maximal effort and HR assessment

A cycloergometer (Excalibur Sport, Lode, Groningen, The Netherlands) was used to induce physical effort. Participants started warming up, cycling with no resistance for 5 min before the incremental test began. The first 2 min-long effort level was set as the participant's bodyweight/2 W (e.g. a participant weighting 70 kgs started with 35 W). Effort was incremented in

bodyweight/2 W steps after each 2-min interval, and the procedure continued until volitional exhaustion. The peak power output (PPO) at the exhaustion point was recorded, and used to classify subjects according to their performance level. Considering the standard guidelines to classify subjects, which is divided in 5 level from 1 to 5 (untrained, recreationally trained, trained, well-trained, and professional, respectively), our sample belonged to the performance level 2 (De Pauw et al., 2013).

The heart rate was monitored using a Polar RS800CX wrist device (Polar Electro Oy, Kmpele, Finland), set to measure pulse rate. Data were transferred to the Polar Protrainer Software. Maximal heart rate, as measured at exhaustion, was later used to calculate reserve heart rate (RHR) in the two experimental sessions.

Submaximal physical-effort task

The main part of each of the two experimental sessions consisted of cycling for 60 min while performing the mental workload task (2-back, oddball version). The rest of the measures (oculo-visual parameters and subjective mental workload) were taken before and/or after this task (see details below).

Before cycling, the participant was asked to lie in a supine position in a quiet room for 6 min and the HR after this resting period was established as HR_{min} . The HR_{max} was computed in the previous session (maximal effort test; see above), and the two HR_{min} measures (one for each session) were used to calculate the reserve heart rate (RHR) for each individual. The 60% of the reserve heart rate is calculated using the Karvonen equation as $[(HR_{max} - HR_{min}) \times 0.6] + HR_{min}$ (Karvonen et al., 1957). Just after the HR assessment, participants performed visual tests (NPC, near stereo acuity, accommodative facility, and eye-hand coordination) before starting the main experimental task.

The participant was then asked to start cycling at bodyweight/2 W. Resistance was increased in bodyweight/2 W steps per min until reaching $60\% \pm 5\%$ of RHR and this level of effort was then held constant for 60 min. Participants were asked to continue cycling at a frequency between 50 and 70 rpm for the entire session, and the current pedalling rate was continuously shown on the cycloergometer display. When HR was higher than 65% of the RHR the resistance was manually decreased in bodyweight/4 W steps per min until reaching $60\% \pm 5\%$ of RHR again. After 60 min of exercise, participants performed 2 min of active recovery at bodyweight/2 W. Just afterwards, NASA-TLX and visual measures were taken.

Mental workload tasks

The cognitive task corresponding to each experimental condition was run simultaneously to the submaximal physical task described above, and started upon reaching the $60\% \pm 5\%$ of RHR.

The mental workload task (60min) was split into blocks of 105 seconds (2-back or oddball), followed by a mental rest period. The recesses were 15 s long for the first two blocks and 75 s for the third block, and this sequence was maintained for the entire 60-min session. The long rest periods (75 seconds) were used to allow participants to freely drink water. The physical task was not interrupted during recesses. All participants performed 25 complete blocks, and this was therefore the total number of blocks considered to check cognitive involvement and performance.

The mental workload task (a 2-digit load version of the N-back task, Owen et al. 2005) consisted of a series of digits (1, 2, or 3), presented randomly, one at a time and at a rate of one digit every 2500 ms (each digit was presented for 1000 ms, and the inter-stimulus interval was 2000 ms). In each trial, the participants were asked if the digit currently on screen was the same as the one presented 2 positions earlier, and they were requested to press a button each time a match was observed (participants did nothing if there was no match). This task thus requires keeping the last two digits in working memory (working memory load), comparing every new digit with the earliest of them (checking), incorporating the new item and discarding the earliest one for further comparisons (updating). The task can be manipulated to raise or lower the working memory load, depending on the number of digits that the participant must keep in mind (2 in the current version of the task).

The oddball condition was designed to be perceptually identical to the 2-back task (Luque-Casado et al., 2015). This condition allowed us to control the potential influence of stimulus setting features (e.g. stimulus duration, inter-stimulus interval, see Luque-Casado et al. 2015). Before the task started, a randomly single digit (1, 2 or 3) was presented on the screen, and the participant was instructed to press the button every time that the digit appeared on the screen during that session, and to withhold the response for the other 2 digits. This task imposes little or no working memory load, but uses exactly the same stimuli as the 2-back task, requires vigilance during the whole session, and the same rate of response (on average, one response/3 trials).

Stimuli of the cognitive load tasks were displayed on a 1920 x 1080 LCD monitor, situated 3 m in front of the participant in order to avoid sustained accommodation ($\sim 0D$), while the participant was cycling. Visual stimuli subtended 8.83 min of arc, which corresponds to 0.11 visual acuity, and were thus clearly visible for any participant of this study. Illuminance of the room was quantified with an Illuminance meter T-10 (Konica Minolta, Inc., Japan), and kept constant during the entire experiment (*mean* \pm *SD*; 249.04 ± 6.47 lux). While cycling, participants held a clicker

on their dominant hand to make the responses required for the cognitive task, and a distinctive sound was used as feedback for each response.

Cognitive performance calculation

Regardless of the task (2-back or oddball) each response qualified as a hit (correct click), a false alarm (or commission error, incorrect click), a correct rejection (correctly non-clicking), or a miss (omission error, incorrectly non-clicking). To check the involvement and performance in the cognitive task, we computed the number of hits, misses, false alarms, and correct rejections in each block. For this, we calculated the hit rate h (hits/total number of go trials) and the false alarm rate f (false alarms/ total number of no-go trials) for the entire mental task. Participants performed a total number of 25 blocks, and for analysis we divided them into five equal parts (phase), resulting in five phases of 5 blocks each. A composite measure of discriminability is the arcsine of f minus the arcsine of h . The larger difference of arcsines, the better performance in the task (Perales et al., 2005).

Visual function

All visual measures were performed before physical and cognitive effort, and just after 2 min of active recovery upon reaching 60 min of physical/mental task. Here, we explain the assessment procedures for the visual parameters: a) The near point of convergence was measured before exertion and after 2 min of active recovery in both experimental sessions. The methodology used was described above (see general visual assessment), and average value from three measures was considered for analysis. b) Near stereoacuity was measured with Randot test, as described above (see general visual assessment), while participants wore glasses with polarized filters. c) The accommodative facility was tested using the Hart Charts under binocular conditions and the procedure was described in the general visual assessment section. And d) eye-hand coordination was tested by a standardized program using the Wayne Saccadic fixator (Wayne Engineering, Skokie, IL, USA). Participants performed a test developed by Dr. Jack Gardner, which takes proaction and reaction times into account for accurate and repeatable rapid testing. The lights start moving at the speed of 60 lights per min, and this speed is increased after each correct response. This programme takes 30 sec, after which the number of correct responses, the average speed, and the final speed in lights/min are displayed. The final score was calculated as the product of number of correct responses and the final speed (Vogel & Hale, 1990). All testing was performed under photopic illumination conditions.

Subjective mental workload assessment (NASA-TLX)

An assessment of mental workload with the NASA-TLX scale (Hart & Staveland, 1988) was carried out only after active recovery. The NASA-TLX is composed of six subscales: Mental demand (How much mental and perceptual activity was required?), Physical demand (How much physical activity was required?), Temporal demand (How much time pressure did you feel due to the rate or pace at which the tasks or task elements occurred?), Performance (How successful do you think you were in accomplishing the goals of the task set by the experimenter?), Effort (How hard did you have to work to accomplish your level of performance?), and Frustration level (How insecure, discouraged, irritated, stressed or annoyed vs. secure, gratified, content, relaxed or pleased did you feel during the task?). The participants were asked to provide scores for each subscale (ranging from 0 to 100). Scores for each subscale, and a weighted total workload score were determined following standard instructions.

Procedure

Participants took part in four sessions. Prior to the first one, held at the Vision Science and Applications Lab at the Optics Department, University of Granada, all volunteers were informed about the experimental aims and conditions, and signed an informed-consent form. Subsequently, the visual system of each participant was assessed to check for the inclusion criteria, as explained above. In this same session, the participants were given instructions and practice with the cognitive task, and the NASA-TLX scale, so that all athletes were familiar with them before the commencement of the study. After verbal explanation, participants were given 5 min to practice with both mental workload tasks.

The second session was carried out at the Motor Behaviour Lab of the Sports Sciences Faculty, University of Granada, and consisted of the incremental maximal effort test to establish maximum HR, as described above. The session was conducted in the presence of a medical doctor, and a defibrillation device was also on hand. This session was used for a definitive RPE calibration, for answering any questions about using the scale, and to encourage participants to focus on an overall perception of effort.

The third and fourth sessions constituted the primary focus of the study (see **Figure 21** for a graphical overview) in which two dual tasks of the same physical effort were performed but each was accompanied by different working -m of 48 h and a maximum of 96 h and both sessions were scheduled at the same time of the day and conducted in a counterbalanced order. Also, the order in which ocular parameters were tested was counterbalanced within-participants.

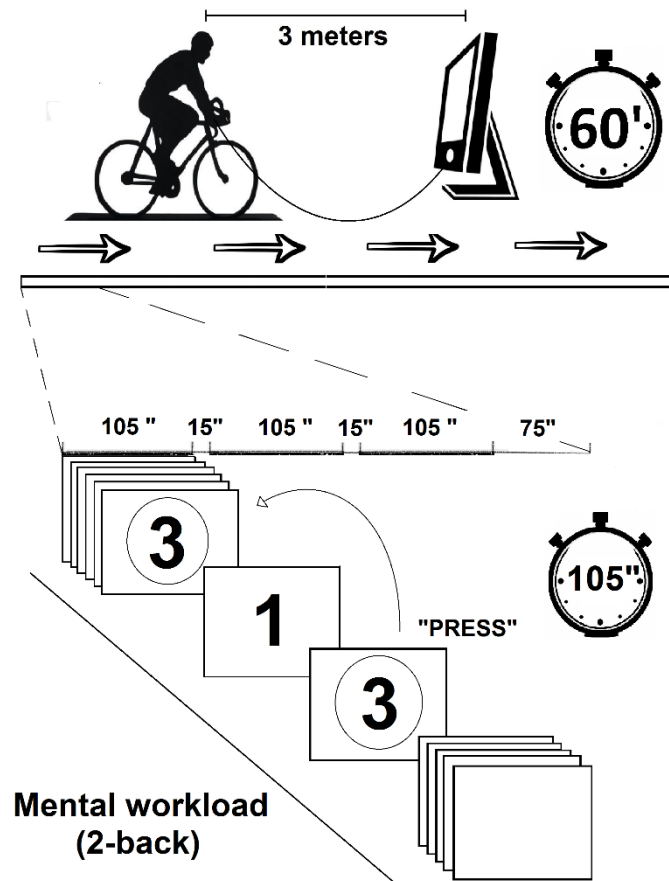


Figure 21. Schematic illustration of the experimental setting during the two main sessions with an example for the mental workload task (2-back). The top part displayed the participant’s disposition in the study. Just below it, a temporal representation of the first three blocks. On the bottom of the figure, appears an example of one block of the mental workload task (2-back). We represent how participants should press in that situation since the number (3) matched with the number (3) displayed two positions before. Instructions for the two cognitive tasks were provided: for the oddball condition, participants read the instructions “press the button when the number X (1, 2 or 3) appears on the screen”. For the mental workload task (2-back), participants read the instructions “press the button when the number on the screen matches with the number presented two positions before”.

Statistical analysis

To check normality of data samples, we submitted all variables tested to the Shapiro-Wilk test, and all showed a normal Gaussian distribution.

To test the cognitive performance and involvement in the cognitive task, we used a composite measure of discriminability [$\arcsines(f) - \arcsine(h)$]. This difference of arcsines was submitted to a 5 (phase) x 2 (cognitive complexity: oddball, 2-back) ANOVA with the two factors as within-participants. To analyze the effect of mental task in subjective mental workload perceived (NASA-TLX), we also performed a *T-test* for related samples for the six NASA subscale and the average score, considering the *mental task* as the within-subjects factor.

To ascertain that both sessions required the same physical effort, we performed two *T-test* for related samples for HR and weighted averaged W/Kg, considering the *mental task* as the within-subjects factor.

Visual measures were analysed individually. ANOVAs were carried out for the break and recovery value of the near point of convergence (NPC), near stereo acuity, accommodative facility (Hart Chart) with the measurement moment (pre-post physical effort) and mental task (oddball, 2-back) as within-participants factors. Finally, we tested eye-hand coordination using an ANOVA for the calculated final score (number of correct responses x final speed) and considering measurement moment (pre, post) and mental task (oddball, 2-back) as within participants-factor. In all cases, we used the Bonferroni-correction for multiple comparison.

The statistical analysis was implemented in SPSS22 IBM software, and a value of .05 was adopted to determine significance.

Results

Cognitive manipulation check

Cognitive performance and subjective responses were used to examine the effectiveness of mental manipulation, as has been done in previous investigations (Siegenthaler et al., 2014). Firstly, we carried out an ANOVA considering the 5 equal phases as the measurement moment and the two mental tasks as within-subjects factor. This analysis showed a significant effect of the mental task [$F(1,17)=163.39$, $MSE=0.033$, $p < 0.001$] (see **Figure 22**). However, the measurement moment or the interaction revealed no significance [$F(4,68)=0.39$, $MSE=0.003$, $p=0.747$ and $F(4,68)=0.243$, $MSE=0.002$, $p=0.89$, respectively]. As expected, the mental workload version gave lower discriminability values than did the oddball version. The scores found in the mental workload version, as well as the oddball version, were well above 0, and therefore the constant involvement of participants in cognitive tasks is clear.

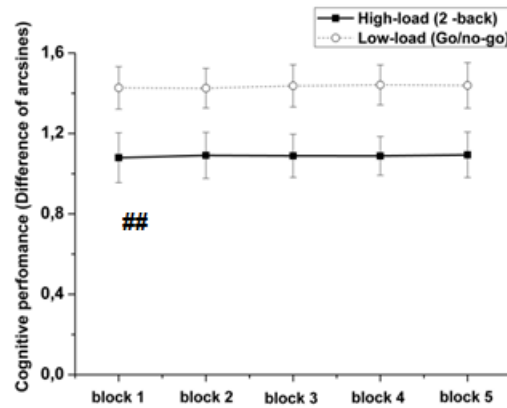


Figure 22. The effect of the cognitive-task level on discriminability score. Average discriminability value for each cognitive-task level (y-axis). The x- axis displays the number of the different phases used with analysis purposes. Data from the oddball condition are represented with open circles and from the mental workload condition with filled squares. ## indicates significant main effect of mental task level (p -value<0.01). Error bars represent the standard deviation (SD) across participants (n=18).

Similarly, participants reported higher mental demand in the corresponding NASA-TLX subscale for the mental workload task than in the oddball task, also the average value for the six NASA-TLX subscales was judged to be higher in the session with mental workload [$t(17)=-7.99$, $p<0.001$, and $t(17)=-2.45$, $p=0.025$, respectively; see **Table 10**].

Table 10. NASA-TLX scores across cognitive-task level and subscales. Average \pm Standard Deviation of NASA-TLX subscales and average score for both mental tasks, calculated from all participants (n=18). Values range between 0 and 100 and higher scores indicate higher perceived task load.

NASA-TLX	Oddball	Mental workload (2-back)	p-value
Mental demand **	25.28 \pm 17.61	60.88 \pm 20.37	<0.01
Physical demand	58.33 \pm 21.07	53.82 \pm 16.35	0.32
Temporal demand	62.22 \pm 20.45	59.71 \pm 14.09	0.6
Performance	29.17 \pm 24.63	38.82 \pm 21.5	0.23
Effort	55 \pm 18.47	56.76 \pm 17.92	0.68
Frustration level	21.67 \pm 19.4	27.94 \pm 18.15	0.38
Average NASA-TLX score *	41.94 \pm 13.73	49.66 \pm 9.28	0.025

Note. * $p < 0.05$ and ** $p < 0.01$

Physical manipulation check

The heart rate was kept at $60\% \pm 5\%$ of the reserve heart rate and was matched between experimental sessions [146.43 ± 6.57 for the oddball condition and 146.72 ± 6.21 for the mental workload condition; $t(17)=0.558$, $p=0.656$], this analysis highlights that the mean HR did not differ between sessions. Also, there were no differences in objective physical output. A *T-test* for related samples across mental tasks on weighted average was far from showing significance [133.72 ± 28.48 W/kg for the oddball, and 132.93 ± 27.8 W/Kg for the 2-back; $t(17)=-0.453$, $p=0.584$]. Therefore, physical demand between sessions were matched, as showed by heart rate and power output.

Effects of physical effort and cognitive task level on visual indices

Figure 23 displays the effect of physical/mental effort in all the parameters tested. An ANOVA considering *mental task* (oddball, 2-back) and *measurement moment* (pre, post) as the within-participants factor showed a major effect of concomitant physical and cognitive effort at the moment of measurement (before and after task) for the break and recovery value of NPC [$F(1,17)=30.75$, $MSE=1.033$, $p<0.001$ and $F(1,17)=21.592$, $MSE=2.607$, $p<0.001$, respectively]. The effect of the mental task displayed a significant difference for the break point [$F(1,17)=4.579$, $MSE=1.317$, $p=0.047$] and a marginal significant difference for the recovery point [$F(1,17)=3.705$, $MSE=1.928$, $p=0.071$]. The interaction *mental task x measurement moment* was far from showing any significance [$F(1,17) < 1$ for break and recovery values]. Our analysis showed that NPC (break and recovery) was impaired as a consequence of concomitant physical and mental effort, regardless of the cognitive-task complexity (oddball, 2-back) [corrected p-values <0.001 , for the break point and the recovery point in both experimental sessions].

Near stereoacuity decreased after physical and cognitive effort. There was a significant main effect of *measurement moment* on near stereopsis [$F(1,17)=5.091$, $MSE=177.39$, $p=0.038$] and a marginal significant effect of *mental task x measurement moment* [$F(1,17)=3.317$, $MSE=100.592$, $p=0.086$], but the *mental task* did not show any significance [$F(1,17)=1.072$, $MSE=236.213$, $p=0.315$]. The mental workload condition elicited a significant change on near stereopsis [$p=0.006$], whereas concomitant physical effort with the oddball task promoted no significant changes on this parameter [$p=0.52$].

For the accommodative facility, we found a significant effect of measurement moment on cycles per min with the Hart Charts [$F(1,17)=21.761$, $MSE=4.831$, $p<0.001$]. However, *mental task* or the interaction (*mental task x measurement moment*) yielded no significance [$F(1,17)=0.68$, $MSE=9.007$, $p=0.421$ and $F(1,17)=0.005$, $MSE=2.602$, $p=0.943$, respectively]. The two

experimental conditions showed an effect (increase) of the measurement moment independently of the mental task performance [correct p -values < 0.01 for both conditions].

Finally, an ANOVA for repeated measures using *mental task* (oddball, 2-back) and *measurement moment* (pre, post) demonstrated a significant interactive effect (*mental task* \times *measurement moment*) for eye-hand coordination [$F(1,17)=5.954$, $MSE=466385,654$, $p=0.026$], but mental task and measurement moment showed no significance [$F < 1$ for both]. A significant effect was found after 60 min of resistance exercise with concurrent mental workload demand [$p=0.018$], but no significant changes were found when the oddball task was performed simultaneously to physical exertion [$p=0.207$].

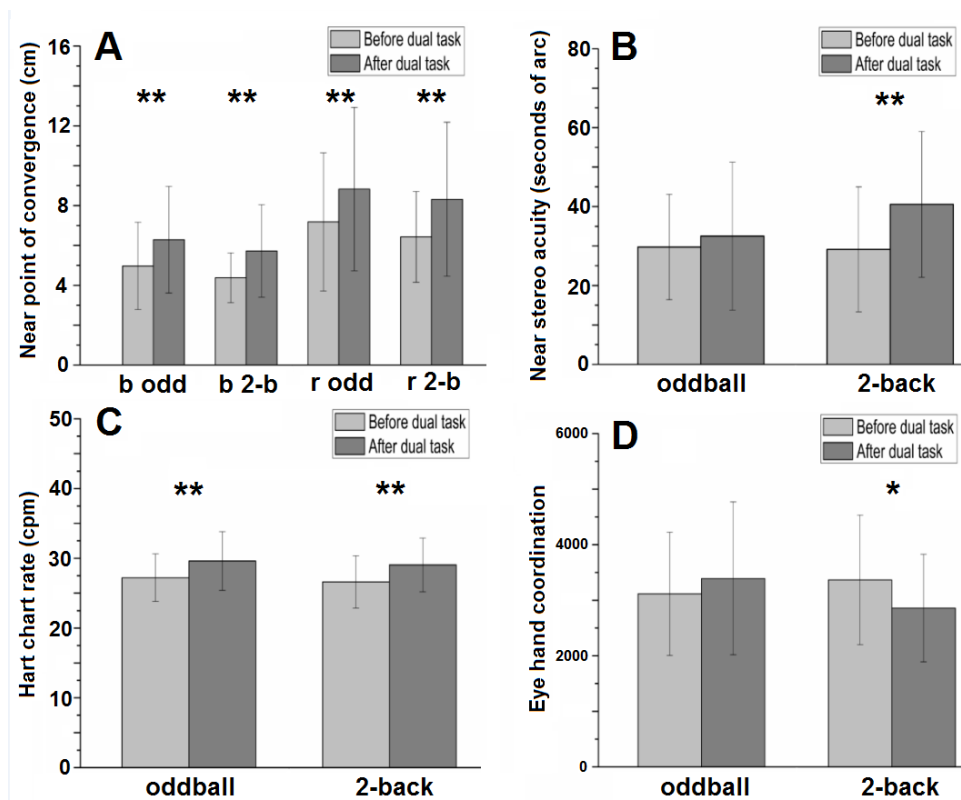


Figure 23. Effect of concurrent physical and cognitive effort on the visual and perceptual-motor skills. A) The effect of physical/mental effort for the break and recovery values of the near point of convergence in both experimental sessions (oddball, 2-back). B) The effect of physical/mental effort for the near stereo acuity in the two experimental conditions (oddball, 2-back). C) The effect of physical/mental effort for the accommodative facility (Hart Chart) under both experimental conditions (oddball, 2-back). D) The effect of physical/mental effort for the eye-hand coordination in the two experimental sessions (oddball, 2-back). Data from the before-exercise measure are indicated in light grey and from the after-exercise in dark grey. “b odd” and “b 2-b” in the panel A represent the break point (b) for the oddball (odd) and the 2-back (2-b) condition, respectively, whereas “r odd” and “r 2-b” indicate the recovery point (r) for the oddball (odd) and the 2-back (2-b) condition, respectively. * and ** indicate statistically significant differences between the moment of measurement (before/ after dual tasking) (p -values < 0.05 and < 0.01 , respectively). Error bars represent the Standard Deviation (SD) across participants ($n= 18$).

Discussion

Simultaneous physical and cognitive tasks promote several significant changes in visual function and eye-hand coordination. This study incorporates several noteworthy findings: the near point of convergence (break and recovery values) moves farther (impair) with physical and cognitive demand irrespective of the complexity of the mental task. Near stereo acuity and eye-hand coordination significantly deteriorated after cycling for 60 min at 60% RHR and performing a mental workload task, but those indices did not change significantly with a matched oddball task. However, accommodative facility improves (higher number of cycles per min) after both session of concurrent physical and mental demand (oddball, 2-back).

We found evidence of a relationship between physical and mental effort and an impairment of near point of convergence. Nevertheless, the mental complexity did not vary the amount of change. This is the first study available to investigate the effect of simultaneous physical/mental demand on the vergence-accommodation system. The related studies in this regard differ on the experimental design and variables analysed. Thus, Hancock & McNaughton (1986) found that under the influence of fatigue, an orienteer's ability to perceive visual information is greatly impaired, and Casanova et al. (2013) demonstrated that prolonged intermittent exercise negatively affects the search behaviour (longer fixations) in soccer players, although high-level players registered less marked decreases. Also, Davies, Wolffsohn & Gilmartin (2005) found a reduction in accommodative response (higher accommodative lag) parallel to increased cognitive demand. However, in our experiment, cognitive demand manipulation was insufficient to find any difference in the near point of convergence. Meanwhile, our experimental manipulation of mental complexity revealed differences for static near stereo acuity and eye-hand coordination. This demonstrates that an added effect of mental workload on physical effort alters visual performance (stereo acuity) and perception-motion processes (eye-hand coordination), while physical and the oddball cognitive task simultaneously induced no changes on those parameters. Hence, mental workload has an effect on the visual system (near stereo acuity) and perceptual-motor skills (eye-hand coordination) that may be considered in dual tasks, particularly important in sport games, but also relevant in other overlapping tasks, such as occupational settings or military operations.

Apparently surprising, our results displayed that accommodative facility increases after physical and cognitive effort, independently of mental workload level. Our explanation for this finding is based on the arousal theory, which approaches the relationship between the activation level (arousal) and the performance in physical and mental activities, indicating that different tasks require different levels of arousal for optimal performance (Dickman, 2002). This complex interaction is known as the inverted-U relationship, first proposed by Yerkes & Dodson (1908) In

accordance with this perspective, Davranche et al. (2006) showed that sub-maximal exercise improves late motor processes (reaction time) in comparison to the resting condition, and the analysis of electromyographic burst suggests that the motor unit discharges better synchronized during exercise. They also found an increase in sensory sensitivity (critical flicker fusion) after an incremental cycling test and ~15 min of cycling at 50% of maximal aerobic power, suggesting an exercise-induced increase in cortical arousal (Davranche & Pichon, 2005). Recently, McMorris et al. (2015) explained that when perception and action are combined, the complexity of the interaction induces different reactions with respect to when cognition is detached from motor performance. Moreover, the activation level determines the performance, and this relationship is different for each type of process. Dual tasks promote related and unrelated homeostatic changes from each one of both demands, and thus it is more complicated to predict the suitable arousal level for each person in a specific situation.

We found that near visual tasks (NPC, stereo acuity, and eye-hand coordination) tended to show impairment after simultaneous physical and mental effort, whereas the only test performed with far demands (accommodative facility) demonstrated an enhancement. Taking these results together, because the parasympathetic innervation dominates accommodation dynamics (McDougal & Gamlin, 2015), we attribute the impairment of near visual tasks to a concurrent reduction in the relative power of the parasympathetic component of the autonomic nervous system during physical and cognitive demand (Davies et al., 2005). Thus, the task with far demands (accommodative facility) could be less affected by autonomic changes due to reduced parasympathetic requirements. Notably, the changes found here in some parameters that characterize the visual function related to the accommodation-vergence system after physical and mental effort exhibit a similar tendency to those changes found after visual fatigue (Poltavski et al., 2012; Thiagarajan & Ciuffreda, 2013), driving fatigue (Vera et al., 2016), alcohol intake (Campbell et al., 2001), cannabinoids consumption (Green, 1998) or sleep restriction (Masuda, Ueda, Nawa, Hara, & Uozato, 2005), all of those changes resulting from the activation state of the nervous system. For example, Poltavski et al. (2012) concluded that in individuals with normal clinical findings of accommodation and vergence this synchrony can break down when doing near tasks under conditions that activate the sympathetic nervous system, and Vera et al. (2016) associated the levels of arousal with variations in ocular signs (decreased intraocular pressure and accommodative response) during simulated driving due to fatigue (e.g. lower arousal levels). Similarly, visual fatigue after task repetition over time reportedly changes the dynamics of the accommodative system (increased lag of accommodation) (Thiagarajan & Ciuffreda, 2013). In addition, the lack of sleep during night shifts decreases accommodative function (Masuda et al., 2005). This background demonstrates that the activation level of the central nervous system is associated with ocular changes. In this sense, as a theoretical explanation, the Central Governor

Model postulates that the brain regulates motor-unit recruitment during demanding effort in order to maintain homeostasis (Noakes, 2012). Hence, physical and/or mental demands can play a role in the ocular system among other structures regulated by the central nervous system.

Future research and current limitations

Jointly, our findings highlight the relationship between the activation level, i.e. from load to fatigue, and variables tested, i.e. from enhancing to impairing. The challenge in future investigation is to understand how those changes impact sport performance, and ascertain the repercussion of sport practice in those capabilities used during game, such as visual skills. This study, conducted in a laboratory setting, is meant to spur further research concerning the effect that physical/mental fatigue exerts on visual skills in ecological settings. The present study considers moderate continuous exercise using a cycloergometer for a period of 60 min with concurrent cognitive demand (oddball, 2-back) and, as stated above, performance depends on activation level and therefore on the type of effort involved. Also, this study has been conducted with male subjects, while differences in the physiological response to exercise between male and female individuals have been documented (Kenney, Wilmore, & Costill, 2015). Consequently, new research with different physical and cognitive protocols, and with females as participants are needed. And lastly, the sensitivity of the instruments used in next studies could be improved by using more precise technology such as open-field autorefractors, wavefront sensors or eye-tracking systems, although integrating those devices into our experimental set-up poses significant technical challenges. In addition, it requires experienced examiners and tedious calibration processes.

Conclusions

The present study indicates that autonomic changes due to physical and mental effort alter accommodation/binocular parameters (near point of convergence, stereo acuity, and accommodative facility) and perception-motion processes (eye-hand coordination). The level of activation (arousal) can enhance or impair the perceptual and perceptual-motor processing depending on the specific parameter tested. Also, it is important to know that when dual tasking (physical and mental) is undertaken, the homeostatic changes are more unpredictable. Therefore, the findings presented here could have an important and direct application in sport contexts in order to enhance performance. Additionally, in future studies should investigate the possible influence of practising demanding exercise in the subsequent activities that require precise visual capacities (e.g. driving, flight operations, surgical procedures, etc.), as well as the potential long-term effect on the ocular health.

CHAPTER VI. DISCUSSION

SUMMARY OF MAIN FINDINGS

The present International Doctoral Thesis has been divided into three sections or ways of addressing the research question (8 studies), and the main findings obtained in each of three sections demonstrate that: 1) Regarding to the influence of physical effort, we have found that subjects who regularly play basketball possess a better visual function and visual information-processing. Nevertheless, further investigation is necessary to elucidate if this better visual function is innate or it is acquired as consequence of constant involvement of the visual system during sport practice. Additionally, we found that stronger individuals present higher intraocular pressure at rest, suggesting a possible influence of the corporal adaptations during strength training on baseline intraocular pressure levels. Lastly, the third study of this section showed an acute effect of strength exercise on IOP (increase), and this variation is linearly associated with the load used (higher load promotes higher IOP rise) and it also depends on the type of exercise performed (higher IOP increments in the bench press than in the jump squat exercise). 2) The investigation of the effect of mental effort on the oculo-visual parameters indicated that these effects may be considered due to effect on task performance (e.g. driving), but also, those ocular parameters such as intraocular pressure, accommodative response, pupil size and ocular aberrations present the possibility to be used as tools to detect the level of mental load/fatigue. Also, the long-term effect of constant mental demanding tasks involvement on the ocular health (e.g. intraocular pressure rise and therefore in glaucomatous damages) needs to be investigated in future studies. 3) The third section was addressed to investigate the effect of concomitant physical and mental effort on the visual system (in terms of ocular physiology as in visual function parameters), the two studies conducted in this perspective demonstrated that a dual (physical/mental) task promotes different changes on the visual system than when each task is administered individually. Moreover, a joint analysis of these tasks is fundamental since they induce ocular alterations in different manner, and it has great importance due to the fact that many daily activities requires physical and mental demand at the same time (e.g. sport games, occupational settings, military operations).

A BRIEF DISCUSSION OF THE MAIN FINDINGS WITH REFERENCE THE RELATED LITERATURE AND THEIR POSSIBLE APPLICATIONS

1. Physical Effort

1.1 Basketball players present better visual abilities than sedentary individuals (Study 1)

This study demonstrates that basketball players exhibit better performance in several visual capabilities than a control group of relatively physically inactive subjects. The better performance in visual skills has been explained from two perspectives, one of them supports an innate superior visual processing ability whereas the other supports the idea that function is improved by constant involvement of the visual system (Del Percio et al., 2007; Jafarzadehpur et al., 2007; Quevedo-Junyent et al., 2011). In this regard, longitudinal investigations could help to resolve these conflicting explanations. Furthermore, the relevance of visual training and its potential application to specific sports may have further relevance since has been reported in previous studies that better visual skills would play a positive role in sporting performance (Erickson, 2007; Gao et al., 2015)

1.2 Stronger individuals suffer from higher baseline intraocular pressure (Study 2)

Subjects with greater force-velocity parameters and maximum dynamic strength (*1-RM*) obtained from the ballistic bench press present with higher baseline IOP values. Taking into account our results and the previous investigations, we suggest that any condition which promotes cardiovascular alterations, such as strength condition in this study, could raise intraocular pressure values (Alan et al., 2003; Bertovic et al., 1999; Di Francescomarino et al., 2009; Miyachi et al., 2004). These results should be considered relevant in the context of glaucoma patients or any circumstances in which IOP behaviour is of significant concern. Also, further research is required to test the consequence of strength training on ocular health, since strength training has been reported to produce potentially unfavourable cardiovascular effects.

1.3 The performance of strength exercises induces an instantaneous rise in intraocular pressure (Study 3)

Strength exercises cause an acute increase in IOP according to the load used and the type of exercise performed. We consider that the position adopted to execute the exercise and the possible involuntary Valsalva Manoeuvre could have an influence on the IOP modifications (Rüfer et al., 2014; Vieira et al., 2006). The possible glaucomatous damage caused by cumulative long-term

intermittent IOP elevations should be approached in further investigations (Schuman et al., 2000). Our findings may have a potential impact on the type of exercise prescribed to glaucoma sufferers or at risk groups.

2. Mental Effort

2.1 Intraocular pressure is sensitive to mental workload (Study 4)

IOP reflects autonomic variations due to cognitive processing (Brody et al., 1999; Vera et al., 2016), as has been corroborated with well-documented indices sensitive to the nervous system's activation state such as heart rate variability (Luft et al., 2009; Luque-Casado et al., 2015) and pupil dynamics (Klingner et al., 2011; Murphy et al., 2014; Wang & Munoz, 2015). Likewise, the autonomic nervous system regulates the intraocular pressure levels (Neuhuber & Schrödl, 2011), thus, central nervous system variations as a consequence of cognitive processing are reflected in IOP behaviour. In this study, we established a promising ocular candidate (IOP) to assess mental workload. It is our hope that this basic research could be applied to ecological settings away from the well-controlled laboratory conditions. In this regard, we believe that a suitable first step was proposed in our fifth study where this variable was measured in a simulated driving context.

2.2 Accommodative response and intraocular pressure reveals driving fatigue (Study 5)

Accommodative response and intraocular pressure decrease with driving time, whereas fatigue levels increase. These changes are explained by the nervous system's activation state, which plays a fundamental role in the regulation of ocular function (Gilmartin, 1986; Kiel et al., 2011; Schor et al., 1999). Our study provides original data on the validity of accommodative response and intraocular pressure as safety indices in driving. Future studies are needed to determine whether accommodative response and intraocular pressure can be used as a fit-for-purpose test, and we also encourage the utilisation of contact lens sensors for continuous IOP monitoring that could lead to a driver fatigue monitoring system based on a wearable device (De Smedt et al., 2012).

2.3 A novel ocular index to assess the effect of cognitive processing (Study 6)

The level of mental task complexity has an effect on the astigmatism aberrations RMS, and it does not have pupillary dependence when pupils were scaled up to 5 mm. A plausible physiological explanation is that the shift from low to high mental workload may be revealed by changes in activity of the autonomous nervous system (Miyake et al., 2009; Trimmel et al., 2009), which modulate ocular physiological parameters such as pupil size, ocular accommodation, and

intraocular pressure, being those factors tightly linked to ocular aberrations. This result could incorporate a promising objective, valid, and reliable index to evaluate the impact of cognitive processing in real contexts. Future research is guaranteed in this regard.

3. Concomitant Physical and Mental Effort

3.1 Intraocular pressure responses to simultaneous physical/mental effort and predicts subjective sensitivity to physical exertion (Study 7)

Our results prove that IOP increases after a dual task (physical/mental), and show that a more demanding mental workload further raises IOP. This study also makes an interesting new discovery which is that IOP partially predicts effort tolerance. The relationship between central nervous system activity and intraocular pressure can regulate IOP behaviour depending on the demands of the task undertaken, and therefore, the nervous system's activation state (Bill, 1975; Kiel et al., 2011; Vera et al., 2016). Since, a broad range of daily tasks have overlapping physical and mental requirements, our two findings have a great relevance for IOP management and application in the field of sport physiology and psychology.

3.2 Variations in visual function during a concomitant physical and mental task (Study 8)

Simultaneous physical and mental effort alters visual function and eye-hand coordination in different directions (from impairment to enhancement) depending on the level of activation (arousal) and the parameter tested. It is well-established that different arousal levels can facilitate or hamper the performance of tasks, and it also depends on type of process (Dickman, 2002; McMorris et al., 2015). Therefore, when combining physical and cognitive demands is important to consider the effect of this dual task on visual function and processing. Jointly, our findings highlight the relationship between the activation level, i.e. from load to fatigue, and variables tested, i.e. from enhancing to impairing (Yerkes and Dodson 1908).

LIMITATIONS AND STRENGTHS

Limitations

This International Doctoral Thesis presents several limitations that must be discussed. In the studies 5, 6 and 7, we consider that when testing the effect of driving and simultaneous physical and mental effort on oculo-visual parameters, respectively, an additional control group would help to obtain more solid conclusions. Future studies should include this in their experimental designs. Additionally, only men were included in the studies 1, 2, 3, 6 and 7 because, for example, in studies 3, 6, and 7 it was difficult to find enough women that met the inclusion criteria which meant that the study was confined to male subjects. Meanwhile, study 1 was conducted with military combat helicopter pilots belonging to the Spanish Army Airmobile Force (FAMET), in which there is only one female member (Attack Helicopter Battalion BHELA I), and study 2 was also carried out with military officers belonging to the Spanish Army Training and Doctrine Command, and no women voluntarily agreed to participate in this experiment. Therefore, whilst we only considered men for those investigations it is our hope that future work will consider women in their experiments. Additionally, due to the fact that our experimental settings and the current technology available did not allow the continuous recording of some indices tested in our investigations, the inclusion of new technologies that permit the continuous monitoring of the oculo-visual parameters (e.g. contact-lens sensor for IOP monitoring, Mansouri, Weinreb, & Liu, 2015) would improve the knowledge of the behaviour of the ocular system in response to those demanding tasks investigated in this thesis. Lastly, some of our results are discussed specifically in terms of central nervous system and ocular function, thus, the inclusion of more autonomous indices (e.g. blood pressure, ocular blood flow, gases exchange, saccadic dynamic, etc), beyond the heart rate or pupil size used in our investigations, would provide further useful data.

Strengths

The main strength of this line of research is the constant implication of specialists from all the disciplines involved in the different studies. An exhaustive control of physical, psychological and visual aspects that could reduce the control of the hypotheses addressed is guaranteed in the different studies. We also consider that our research has a direct application to society, focusing on the effects of the recurrent involvement on those types of tasks investigated here (physical, mental or a combination of both) in ocular health and accident prevention.

FUTURE DIRECTION IN RESEARCH

The potential impacts that our investigation could have in improving operator's safety (e.g. drivers, helicopter pilots) or patient's safety (e.g. surgeons), as well as for the prevention or control of eye diseases (glaucoma) provides us with an incentive to continue with this line of research. We are currently conducting further studies in this area which we have been unable to include in this thesis, specifically, we are investigating the impact of cognitive demand in military helicopter pilots and surgical residents during simulated flight procedures and surgical operations in order to enhance operator and patient's safety, respectively. In terms of further progress, the next step would be to develop technology capable of monitoring the effect of physical and/or mental effort in the visual system in order to provide a fit-for-duty test e.g. for drivers, aviators, surgeons, athletes and other real-life applications for this technology.

CONCLUSIONS

From this International Doctoral Thesis we can conclude that:

1. There is a relationship between upper-body strength capabilities and baseline intraocular pressure, suggesting that corporal adaption processes as a consequence of strength training have an effect on intraocular pressure. These findings have great importance in terms of ocular health and glaucoma management.
2. Performing strength exercises induces an acute increment in intraocular pressure, with higher changes when executing bench press in comparison with the squat exercise at the same relative intensities. The supine position of the bench press compared to the standing position of the squat could be responsible of the higher increase in IOP during the bench press throw. It has a great application in fitness exercise prescription for intraocular pressure management, and investigating the possible long-term effect of strength training on glaucomatous damage is necessary in further experiments.
3. Individuals with an active sporting background, basketball players in our case, show a better performance in several visual capabilities in comparison with a group of sedentary, physically inactive participants.
4. Intraocular pressure is sensitive to the level of mental workload, showing an association between IOP and nervous system activation state. This finding permits the development of new neuroergonomic tools to detect mental state in real contexts.
5. Driver fatigue is reflected in accommodative response and intraocular pressure suggesting that the ocular system signals the nervous system's activation state, and providing a possible useful measure of driver fatigue that could be implemented in real scenarios.
6. Higher mental workload demand induces a significant increment in the astigmatism aberration. These findings may open up a new possibilities concerning the use of astigmatism aberration as an indicator of mental workload level with interesting applications in ecological situations.
7. Performing a dual task (physical/mental) results in intraocular pressure changes (higher values), and increasing the level of mental demand promotes an additional effect on intraocular pressure variations. Also, there is evidence that intraocular pressure partially predicts

subjective effort perceived. These results are of interest in the field of optometry and ophthalmology (IOP behaviour) and sports physiology and sports psychology (predictor).

8. The autonomic changes due to physical and mental effort alter visual function and eye-hand coordination, demonstrating a specific effect depending on the level of mental demand implemented during resistance exercise. The visual and the visual-motor processing can be enhanced or impaired according to the specific parameter tested.

CONCLUSIONES

De esta Tesis Doctoral Internacional podemos concluir que:

1. Hay una relación entre las capacidades de fuerza del tren superior y la presión intraocular basal, sugiriendo que los procesos de adaptación corporales como consecuencia del entrenamiento de fuerza tienen un efecto en la presión intraocular. Estos hallazgos tienen una gran importancia en términos de salud ocular y el manejo del glaucoma.
2. La realización de ejercicios de fuerza induce un aumento agudo de la presión intraocular, con mayores cambios cuando se ejecuta el press de banca en comparación a la sentadilla con las mismas intensidades relativas. La posición supina adoptada durante el press de banca comparada con la posición erguida de la sentadilla podría ser la responsable del mayor incremento de la presión intraocular durante el press de banca. Esto tiene una gran aplicación en la prescripción de ejercicio para el manejo de la presión intraocular, y la investigación del posible efecto a largo plazo del entrenamiento de fuerza en daños glaucomatosos es necesario llevarlo a cabo en futuros experimentos.
3. Individuos que han sido físicamente activos en el pasado, jugadores de baloncesto en nuestro caso, muestran un mejor rendimiento en varias habilidades visuales en comparación a un grupo de individuos sedentarios.
4. La presión intraocular es sensible al nivel de carga de trabajo de mental, mostrando una asociación entre presión intraocular y el estado de activación del sistema nervioso central. Este resultado permite el desarrollo de nuevos instrumentos neuro-ergonomicos para detectar el estado mental en contextos reales.
5. La fatiga en conducción se manifiesta en la respuesta acomodativa y la presión intraocular, sugiriendo que el sistema ocular señala el estado de activación del sistema nervioso, y provee de una posible medida útil de fatiga en conducción que podría ser implementada en escenarios reales.
6. Una mayor demanda de carga de trabajo mental induce un incremento significativo de la aberración astigmática. Estos hallazgos podrían abrir nuevas posibilidades relacionadas con el uso de la aberración astigmática como un indicador del nivel de carga de trabajo mental con interesantes aplicaciones en situaciones ecológicas.

7. Realizar una tarea dual (física/mental) da lugar a cambios en la presión intraocular (valores superiores), y aumentar el nivel de demanda mental promueve un efecto adicional en las variaciones de presión intraocular. También, hay evidencia de que la presión intraocular parcialmente predice el esfuerzo percibido subjetivo. Estos resultados son interesantes en el campo de la optometría y oftalmología (comportamiento de la presión intraocular) y fisiología y psicología del deporte (predictor).

8. Los cambios del sistema nervioso autónomo debido al esfuerzo físico y mental alteran la función visual y la coordinación ojo-mano, demostrando un efecto específico dependiendo del nivel de demanda mental implementado durante el ejercicio de resistencia. El procesamiento visual y visuo-motor pueden ser potenciados o deteriorados dependiendo del parámetro específico medido.

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AGRADECIMIENTOS

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Table 9. NASA-TLX scores across cognitive task level and subscales. Average \pm Standard Deviation, of NASA-TLX subscales for both mental levels, calculated from all participants (n=17). Values range between 0 and 500. Higher scores indicate higher perceived task load. * indicates statistically significant differences between the measuring session, $p < 0.05$.

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Figure 1. The original version of the Yerkes-Dodson law (Yerkes & Dodson, 1908). This version, based on the actual findings and theorizing of Yerkes and Dodson, takes into account that during simple task (dotted line) the subject can maintain an optimal performance over the entire range of arousal but the complex task (straight line) can be impaired in performance with high arousal levels. Figure 1 is adapted from Figure 2 of Diamond, Campbell, Park, Halonen, & Zoladz, (2007).

Figure 2. Schematic illustration of the structures involved with aqueous humour formation and outflow. Figure 2 is retrieved from figure 23 of McDougal & Gamlin (2015).

Figure 3. Representation of accommodative response curve as a function of accommodative demand. The dotted line represents the ideal response, and the red line shows a classic accommodative response in general population, indicating a lag of accommodation. Figure 3 is retrieved from figure 1 of López-Gil et al. (2013).

Figure 4. Representation of ocular aberrations formation, showing the first 15 Zernike terms and their corresponding far field point spread functions (PSF). Figure 4 is adapted from figure 3 of (Vera-Díaz & Doble, 2012) and figure 5 of (Einighammer et al., 2009) .

Figure 5. Visual discrimination index (VDI) diagrams of two participants belonging to each experimental group (basketball player number 11, and sedentary participant number 4). Data in green represent correct responses: numbers 1 and 2 indicate if the stimulus was identified just once or both times, respectively. Red crosses indicate that no stimulus was identified in that position.

Figure 6. Force-Velocity relationship of a representative participant of the study sample. F_0 , theoretical maximal force; V_0 , theoretical maximal velocity; P_0 , theoretical maximal power. P_0 was calculated as $(F_0 \cdot V_0)/4$.

Figure 7. Linear regression analysis showing the correlation between the baseline intraocular pressure (IOP) and the theoretical maximal power (P_0). Open circles represent data for the entire sample (n=23). ($P < .01$, $r_{23} = 0.557$).

Figure 8. A) Effects of performing jump squats at different intensities on IOP. B) Linear regression analysis showing the correlation between intraocular pressure and the four absolute loads used. In the panel A) the mean intraocular pressure in the baseline reading and just after exercise in the four consecutive loads are displayed. Panel B) illustrates the linear association of intraocular pressure with the four loads implemented ($y = 6.05x + 0.16$; $r^2 = 0.88$). The x-axis

shows the moment of measurement, considering the baseline assessment (panel A) and the relative loads. ** indicates statistically significant differences between the measurement (corrected p-value < 0.01). Errors bars represent the Standard Error (SE). All values are calculated across participants (n=17).

Figure 9. A) Effects of performing ballistic bench press at different intensities. B) Linear regression analysis showing the correlation between intraocular pressure and the four absolute loads used. In the panel A) the mean intraocular pressure in the baseline reading and just after exercise in the four consecutive loads and the one maximum repetition are displayed. Panel B) represents the linear association of intraocular pressure increase with the four loads implemented ($y = 10.26x + 0.13$; $r^2 = 0.94$). The x-axis shows the moment of measurement, considering the baseline assessment (panel A) and the relative loads. ** indicates statistically significant differences between the measurement moments (corrected p-value < 0.01). Errors bars represent the Standard Error (SE). All values are calculated across participants (n=17).

Figure 10. The effect of the type of exercise on IOP at the same relative intensities. Average intraocular pressure values for each exercise (squat vs bench press) at 50 and 60 %RM. Data from the squat exercise are represented in red and from the ballistic bench press in blue. ** indicates statistically significant differences between the two exercises (corrected p-value < 0.01). Errors bars represent the Standard Error (SE). All values are calculated across participants (n=17).

Figure 11. Schematic illustration of the experimental setting for the two conditions. On panel A (left side) the condition with high mental workload (3-back) is represented (in red). On panel B (right side) the oddball condition is shown (in blue). The two conditions were divided in three blocks of 11 min, with one-min break between blocks used for IOP assessment. Each block was divided in five trails of 105 s with a 15-s rest periods between trials, excepting a 75-s rest period after the third trail. For the 3-back task (panel A), participants read “press the button when the number on the screen matches the number presented three positions before”. In our illustration, participants should press the button since the number (1) matched with number presented three positions before. For the oddball condition (panel B), participants read the instructions “press the button when the number X (from 1 to 3, in our example the number randomly chosen was 3) appears on the screen”.

Figure 12. Effects of task complexity on the cognitive performance, intraocular pressure and HRV. (A) Cognitive performance (B) intraocular pressure and (C) HRV across participants at the two task-complexity levels. Data from the 3-back condition represented in red, and from the oddball task, in blue. In the panel (A) the cognitive performance for the three mental workload blocks are displayed, and higher scores indicate better performance. In the panel (B and C) the

intraocular pressure and the HRV, respectively, show the effect of time on task and task complexity. The x-axis shows the measurement before mental workload, the three continuous blocks of mental workload, and the recovery measurement (5 min) for the panels (B and C). In the panel (C) higher values indicate higher autonomic control. * indicates statistically significant differences between the measurement moments represented with grey lines (corrected p-value < 0.05). ## indicates statistical differences between task-complexity levels (p-value < 0.01). Error bars represent the standard error (SE). All values are calculated across participants (n=14).

Figure 13. A) Effects of driving time on the intraocular pressure. B) Effects of driving time on the accommodative response. Average accommodative lag for each distance to the near target before and after driving session. The accommodative lag indicates the amount of under-accommodation, i.e. the inaccuracy of the focusing system. Here, higher values indicate lower accuracy. The accommodative lag is represented as a positive value for graphical purposes (diopter [-D]). A and B) Data from the Pre-Driving measure are indicated in blue and, from the Post-Driving measure, in red. * indicates statistically significant differences between the measuring sessions (corrected p-values < 0.05). Error bars represent the Standard Deviation (SD) and boxes represent the Standard Error (SE). Both values are calculated across participants (n = 12).

Figure 14. Schematic illustration of the experimental setting for the two conditions. On panel A (left side) the condition with high mental workload (3-back) is represented (in red). On panel B (right side) the oddball condition is shown (in blue). Mental workload tasks were divided in intervals of 105 s long with a 15-s rest periods between trials, excepting a 75-s rest period after the third trail. This sequence was maintained for the entire experimental session. For the 3-back task (panel A), participants read “press the button when the number on the screen matches the number presented three positions before”. In our illustration, participants should press the button since the number (1) matched with number presented three positions before. For the oddball condition (panel B), participants read the instructions “press the button when the number X (from 1 to 3, in our example the number randomly chosen was 3) appears on the screen”.

Figure 15. Effects of mental task complexity on astigmatism RMS for total, internal and corneal aberrations with natural pupils. Data from the 3-back condition represented in red, and from the oddball task, in blue. The x-axis shows the four measurement moments, with the measurement before mental workload, the measurements after 11 minutes and 33 min of mental workload, and the recovery measurement (10 min). # indicates statistical differences between task-complexity levels (p-value < .05). Error bars represent the standard error (SE). All values are calculated across participants (n=12).

Figure 16. Effects of mental task complexity on astigmatism RMS for total, internal and corneal aberrations with 5, 4.5, and 4 mm scaled pupils. The top, middle and bottom rows represent astigmatism RMS in 5, 4.5 and 4 mm scaled pupils, respectively. The left, middle and right columns represent total, internal and corneal astigmatism RMS aberrations, respectively. Data from the 3-back condition represented in red, and from the oddball task, in blue. The x-axis shows the four measurement moments, with the measurement before mental workload, the measurements after 11 minutes and 33 min of mental workload, and the recovery measurement (10 min). # indicates statistical differences between task-complexity levels (p -value < .05). Error bars represent the standard error (SE). All values are calculated across participants ($n=12$).

Figure 17. The effect of mental task complexity on pupil size (PS). Mean value for each measurement moment for the 3-back condition (red) and for the oddball condition (blue) (left y-axis). Errors bars represent the Standard Error Mean across participants ($n=12$).

Figure 18. The effect of cognitive task level on discriminability scores. Average discriminability value for each cognitive task level (y-axis). ## indicates significant main effect of cognitive load (p -value < 0.01). Error bars represent the Standard Error (SE) across participants ($n=17$).

Figure 19. The effects of physical and mental load on intraocular pressure (IOP). Average IOP value for each cognitive task level (y-axis). \$\$ indicates significant main effect of measurement moment (p -value < 0.01). ** and * indicate statistically significant differences between the measurement point (corrected p -value < 0.01 and < 0.05, respectively). Error bars represent the Standard Error (SE) across participants ($n=17$).

Figure 20. Relationship between IOP and fitness level with RPE and SAM valence for each measurement moment and cognitive load. A) Regression coefficients for each RPE measure in the oddball condition; B) Regression coefficients for each RPE measure in the 2-back condition; C) Regression coefficients for each SAM valence measure in the oddball condition; D) Regression coefficients for each SAM valence measure in the 2-back condition. The x-axis displays the different measurement moments during the experiment. “Aft-warm” indicates the measure after 2 minutes of warming up, from 1 to 24 are represented the subjective scales reported by participants after each mental block, “aft-task” means the measure obtained just after finishing the dual task, “act-rec” corresponds to the measure collected after 2 minutes of active recovery, and lastly, “pas-rec” represents the measure after 15 minutes of passive recovery. ** and * indicate statistically significant differences (p -value < 0.01 and < 0.05, respectively). Regression coefficients are calculated across participants ($n=17$).

Figure 21. Schematic illustration of the experimental setting during the two main sessions with an example for the mental workload task (2-back). The top part displayed the participant's disposition in the study. Just below it, a temporal representation of the first three blocks. On the bottom of the figure, appears an example of one block of the mental workload task (2-back). We represent how participants should press in that situation since the number (3) matched with the number (3) displayed two positions before. Instructions for the two cognitive tasks were provided: for the oddball condition, participants read the instructions "press the button when the number X (1, 2 or 3) appears on the screen". For the mental workload task (2-back), participants read the instructions "press the button when the number on the screen matches with the number presented two positions before".

Figure 22. The effect of the cognitive-task level on discriminability score. Average discriminability value for each cognitive-task level (y-axis). The x- axis displays the number of the different phases used with analysis purposes. Data from the oddball condition are represented with open circles and from the mental workload condition with filled squares. ## indicates significant main effect of mental task level (p -value<0.01). Error bars represent the standard deviation (SD) across participants (n=18).

Figure 23. Effect of concurrent physical and cognitive effort on the visual and perceptual-motor skills. A) The effect of physical/mental effort for the break and recovery values of the near point of convergence in both experimental sessions (oddball, 2-back). B) The effect of physical/mental effort for the near stereo acuity in the two experimental conditions (oddball, 2-back). C) The effect of physical/mental effort for the accommodative facility (Hart Chart) under both experimental conditions (oddball, 2-back). D) The effect of physical/mental effort for the eye-hand coordination in the two experimental sessions (oddball, 2-back). Data from the before-exercise measure are indicated in light grey and from the after-exercise in dark grey. "b odd" and "b 2-b" in the panel A represent the break point (b) for the oddball (odd) and the 2-back (2-b) condition, respectively, whereas "r odd" and "r 2-b" indicate the recovery point (r) for the oddball (odd) and the 2-back (2-b) condition, respectively. * and ** indicate statistically significant differences between the moment of measurement (before/ after dual tasking) (p -values <0.05 and <0.01, respectively). Error bars represent the Standard Deviation (SD) across participants (n= 18).

RESEARCH PROJECTS

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1. La condición física como mediador de la carga mental experimentada por pilotos de aviación militares. Ministerio de Economía y Competitividad (DEP2013-48211-R; IP: David Cárdenas Vélez).
2. El ejercicio físico como mediador de la carga mental de los pilotos de helicóptero). Centro Mixto UGR-MADOC (PIN 11; IP: David Cárdenas Vélez).
3. Fatiga al Volante. Mejora de la seguridad visual mediante la prevención de los accidentes debidos a la fatiga: biomarcadores oculares como índices objetivos de fatiga. Dirección General de Tráfico, Ministerio del Interior (SPIP2014-01426; IP: Leandro Luigi Di Stasi).
4. Towards a physician cognitive-load detector based on neuroergonomic indices. CEI BIOTIC (V7-2015, IP: Carolina Díaz-Piedra)

SCIENTIFIC PUBLICATIONS DERIVED FROM THIS DOCTORAL THESIS

1. **Vera, J.**, Díaz-Piedra, C., Jiménez, R., Morales, JM., Catena, A., Cárdenas, D & Di Stasi, LL. (2016). Driving time modulates accommodative response and intraocular pressure. *Physiology & Behaviour*. 164: 47-53.
2. **Vera, J.**, Jiménez, R., Cárdenas, D., Redondo, B & García-García, JA. Visual function, performance and processing of basketball players versus sedentary individuals. (submitted).
3. **Vera, J.**, Jiménez, R., García-Ramos, A & Cárdenas, D. Muscular strength is associated with higher intraocular pressure in military helicopter pilots. (submitted).
4. **Vera, J.**, García-Ramos, A., Jiménez, R & Cárdenas, D. The acute effect of ballistic bench press and jump squat exercises at different intensities on intraocular pressure. (submitted).
5. **Vera, J.**, Jiménez, R., García-García, JA & Cárdenas, D. Intraocular pressure is sensitive to cumulative and instantaneous mental workload. (submitted).
6. Jiménez, R., **Vera, J.**, González-Anera, R., Jiménez, JR & Cárdenas, D. Ocular astigmatism aberration as an objective index of mental workload. (submitted).
7. **Vera, J.**, Jiménez, R., Garcia, JA., Perales, JC & Cárdenas, D. Intraocular Pressure Predicts Subjective Sensitivity to Physical Exertion in Young Males. (submitted).
8. **Vera, J.**, Jiménez, R., García-García, JA & Cárdenas, D. Simultaneous physical and mental effort alters visual function. (submitted)

SCIENTIFIC CONFERENCES

1. The effect of physical activity on the visual system. VIII International Congress of the Spanish Association of Sport Sciences (2014). Caceres, Spain.
2. The influence of physical and mental fatigue on the visual skills used by athletes. I Online International Congress for Young Optometrists (2014). Valencia, Spain.
3. The influence of cognitive effort on intraocular pressure and heart rate variability. A preliminary study. 24 International Congress of Optometry, Contact Lens and Ophthalmic Optics (2016). Madrid, Spain.
4. The effect of executive load on judgments of perceived physical effort and affective valuation during a dual mental-physical task. First meeting of the Society for the Advancement of Judgment and Decision Making Studies (2016). Mallorca, Spain.

RESEARCH STAYS

1. Western University of Health Science, College of Optometry, Pomona, California, United States of America. 117 days.
2. University of California at Berkeley, School of Optometry, Marty Banks' Lab, Berkeley, California, United States of America. 90 days.

