~~Minireview Article~~ Original research article/study protocol

~~1. Visual Impacts of the Digital Environment~~Assessing Retinal Function Alterations Due to Digital Device Use: A Study of Computer Vision Syndrome in Medical Students

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Abstract: Update abstract to include results of key findings

Digital devices, mainly smartphone with its time-consuming applications and 24/7 internet connection, are accused of the being the main cause of severe distraction and excessive disruptions with fragmentation of everyday life that adversely interrupts the adults and youth lifestyles, health, education and social or family relationships. The medical students underwent objective ophthalmic examination to confirm or exclude CVS diagnosis based on Iqbal's four major criteria for accurate CVS diagnosis. Strict reduction or cessation of exposure to blue light for 4 weeks results in spontaneous resolution of cone adaptation/saturation thus eventually the retina regains its normal foveal functions and responses with normal visual acuities and performances.

Keywords: Light emitting diodes; Blue light; Computer vision syndrome; Digital eye strain; Multifocal electroretinogram; Screen-induced foveal dysfunction; Retinal phototoxicity; Retina; Digital environment, digital screens and electronic devices; Iqbal's criteria and instructions. (Limit to 6 key words and arrange in alphabetical order).

Introduction

The innovative digital technology has occupied an enormoustime of the individuals' daily activities and dramaticallyaffected the modern lifestyle [1-5]. The digital environment means

watching and interacting with several types ofdigital devices for extended periods through the entire day [1, 2]. The average screen-time in the digital environments reaches up to eight hours daily for the American adult interacting with ≥10 different types of digital screens [6, 7]. Within the digital environments, the routine exposure to various digital devices and electronic screens for several daily screen-hours has elicited various visual, ocular surface and extraocular symptoms and complaints known as the computer vision syndrome (CVS) or digital eye strain (DES) [1, 3-5]. The American Optometric Association (AOA) defined the computer vision syndrome (CVS) as follows "Computer vision syndrome, also referred to as digital eye strain, describes a group of eye- and vision-related problems that result from prolonged computer, tablet, e-reader and cell phone use" [8].Meanwhile, the Tear Film & Ocular Surface Society (TFOS) considered DES as a more appropriate and specific tem than CVS and further redefined DES as "the development or exacerbation of recurrent ocular symptoms and/or signs related specifically to digital device screen viewing" [1]. CVS is a multifactorial syndrome that affects more than one human system and its sequelae extend beyond the eye [3-5].

The CVS main visual symptoms are visual blur, eye strain/fatigue, seeing unclear objects post-screen use, glare/seeing halos of light around objects, feeling diminution of vision,double vision/diplopia, difficulty in refocusing the eyes, near vision discomfort/difficulty and increased sensitivity to light [1, 3-5, 8-16].The CVS main ocular surface symptoms are dry eye, eye redness,itching/eye rubbing, watery eye, eye irritation/discomfort, foreign body sensation, burning sensation, heavyeyelids and frequent blinking[1, 3-5, 8-16]. The CVS main extraocular symptoms are headache, neck/shoulder/back pain, joint pain in fingers and wrists, inability to hold objects well, difficulty to write using a pen, sleep disturbances/insomnia and inattention [3-5, 8-16]. Other serious manifestations; mainly behavioral and mental health issues, such as

depression, stress, anxiety, tendency to suicide and midnight hunger with weight gain have also been linked to CVS sequelae [3-5, 16-20]. However, both CVS visual and ocular surface symptoms could be attributed to accommodation disturbances, dry eye disease (DED), binocular vision dysfunction and contact lens wearing [1, 3, 4].

Digital devices, mainly smartphone with its time-consuming applications and 24/7 internet connection,~~are accused of the~~ have been implicated as being the main cause of severe distraction and excessive disruptions withfragmentation of everyday lifethatadversely interrupts the adults and youth lifestyles, health, education and social or family relationships [2, 3, 21]. Therefore, such subjects may encounter serious troubles in their lives such aslow productivity, poor creativity and weak academicperformance[2, 21]. However, it seems that the problem is not in the digital device or the smartphoneitself, but the way people handle it and misuse it. In other words, digital devices are not responsible for exacerbation of CVS but the way ~~of its usage~~ and manner it is been used is the actual problem [2-5]. The main risk factors and incorrect practices of the individuals' screen-styles are improper or too close eye-screen distance,screen edge at/above horizontal eye level, improper gaze angle(e.g. when lyingdown or in beds), improper or poor lighting conditions, screen- glare, poor screen- resolution or design, uncomfortable seating postures, watching screen in the dark, small screen-size, excessive screen brightness, small-font size, texting with both thumbs, prolonged screen-hours (average daily screen-hours exceeds five hours) and associated uncorrected refractive errors [3-5]. These risk factors constitute the digital screen or smartphone misuse or abuse practicesthat are responsible for development, exacerbation and aggravation of CVS [3-5].

Methodology:

In ~~our~~ the three published studies by Iqbal et al. [3-5], all medical students responded to the subjective valid and reliable computer vision syndrome form-3 (CVS-F3)questionnaire (.742 Cronbach's alpha reliability coefficient, .773Guttman Split-Half Coefficient and 82% construct validity rate with the Pearson's correlation validity coefficient) that was designed to be ideal for University students [3-5]. The medical students underwent objective ophthalmic examination to confirm or exclude CVS diagnosis based on Iqbal's four major criteria for accurate CVS diagnosis[3-5, 9-13].The complete ophthalmic examination included bothuncorrected and corrected distance visual acuities (UDVA and CDVA; respectively) measurements, testing pupillary reflexes, DED tests, intraocular pressure measurement,subjective and cycloplegic refraction measurements, slit-lamp and dilated fundus examinations [3-5]. The exclusion criteria were amblyopia, strabismus,accommodation-convergence imbalance, near vision abnormalities, anisometropia greater than 2 diopters (D), myopia >6 D, hyperopia >4 D, astigmatism >4 D, eye or retinal pathology, current eye or systemic diseases and previous eye or systemic surgeries [3-5].

Furthermore, the medical students underwent multifocal electroretinogram (mfERG) examination. We used the mfERG device (RETIscan; Roland Instruments, Wiesbaden, Germany) in accordance with the standard protocol for mfERG of the International Society for Clinical Electrophysiology of Vision (ISCEV). The mfERG stimulus used in our studies was 61 hexagons in dilated subjects with system age-matched norms. The protocol adhered to ISCEV standards and our cut-off values were the normal ranges provided by the ISCEV standard protocol.Eventually, we documented the first foveal peak and amplitude density (P1 AD) in all the mfERG Rings and Quadrants.

Note to Author(s)

This is breakdown of what your methodology is:

1. You administered a questionnaire (called CVS-F3) to medical students to assess symptoms of computer vision syndrome (CVS) following the approach established by **Iqbal et al.**

2. The students then had a detailed eye exam to check for signs of CVS. This included:

- Checking vision clarity both with and without corrective lenses,
- Testing how well their pupils responded to light,
- Measuring eye pressure,
- Testing for dry eye,
- Conducting detailed eye exams using equipment to look at the eye's structures.

3. A multifocal electroretinogram (mfERG) was then done to measure the function of the retina. Using RETIscan, how different parts of the retina responded to light was also examined.

Hence, this does not look like a review but an original research article or study protocol.

I expected result for:

1. **Prevalence of CVS Symptoms:**Reporting the frequency and severity of CVS symptoms (e.g., eye strain, dry eyes, blurred vision) among the medical students, as well as their screen usage patterns

2. **Comparison of Visual Function Between Groups**: I expect comparisons of visual functions (uncorrected and corrected vision clarity) between these groups by categorizing students into CVS-positive and CVS-negative groups based on Iqbal's diagnostic criteria.
3. **Retinal Response Differences**: The mfERG test is supposed to reveal differences in retinal function between the CVS-positive and CVS-negative groups.
4. **Impact of Screen Time on Retinal Function**: Since the methodology includes data on daily screen hours, I expect to see if higher screen time correlates with worse retinal function (as measured by mfERG), supporting a dose-response relationship between screen exposure and retinal impact.

I suggest that the author(s) provide the result from this methodology and write a detailed discussion in line with the result from the study.

Outcomes: retinal impacts of the digital environment: There is no result to prove all your assertions in this section. Provide results that was obtained through the methodology.

Wehave exhibited that the digital environment including the digital devices and electronicscreens that contains light emitting diodes(LEDs) that emits blue light, affects the macular integrity as we have already documented the existence of the screen-induced foveal dysfunction (SFD) in our three publishedstudies[3-5]. We are the first ophthalmic team that investigated the mfERGfoveal changes elicited by the exposure to blue light emitting-screens. These mfERG changesexhibitedthe reduction in foveal responses representing the fovealdysfunction that was associated with corresponding reduction in visualperformances and acuities. The SFD was recordedin the university students diagnosed as positiveCVS-caseswho watching digital devices forprolonged screen-hours (>5 average screen-hours) with extensive exposure to varioustypes of

blue light emitting-screenssuch aslaptops, smartphone, pads/tabs and/or desktop devices[3-5].Interestingly, most of these positive CVS-cases were medical students who were involved in the University mandated computer system use program.

Our studies included two groups; the control and the CVS groups. The control groups involved medical students that had no-CVS diagnosis, spending less than threedaily screen-hours on average,exhibited normal mfERG findingsthat revealed within normal preserved foveal peak and mfERG Quadrants and Rings were within ISCEV standard protocol normal ranges. On the other hand, CVS groups included medical students that had positive CVS diagnosis that wasbased on Iqbal's four major criteria for accurate CVS diagnosis [3-5, 9-12], spending more than five daily screen-hours on average, exhibitedabnormal mfERG findingswithstatistically significant foveal amplitude reduction in P1 AD in most of the mfERG Quadrants and Rings below ISCEV standard protocol normal ranges [3-5]. In comparison with the control groups, the CVS groups exhibited a statistically significantfoveal amplitude reduction in the uncorrected and the corrected distance visual acuities (UDVA and CDVA; respectively) [3-5].

Furthermore, we discovered that the SFD is a potential reversible phenomenon [5]. We recorded both the mfERG changes and associated visual acuities before and 4 weeks following strict reduction of the screen-time to≤1 screen-hour daily in both the control and the CVS groups [5]. Thereafter, the medical students in the CVS group exhibited remarkable statistically significant improvements in mfERG foveal responses near to normal ranges with correlated improvements in both UDVA and CDVA [5]. We alsodocumented a positive correlation between the differences of average daily screen-hours reduction and the differences in mfERG Quadrants and Rings P1 AD [5, 10].Therefore, the lower the daily screen-hours with less exposure to the blue light emitted from digital screens, the more the improvements in the foveal responses [10].

Based on our outcomes, we have defined the term screen-induced foveal dysfunction (SFD) as "**the multifocal electroretinogram reduced foveal responses below standard normal ranges that aremostly associated with reduced visual acuities and performances in computer vision syndrome positive-cases**" [3-5, 9-12]. Therefore, SFD could be discovered inpositive CVS-casesand is mostly associated with blurring of vision, feelings of diminution of vision, visualization of unclear objects especially post-screen use, feeling the diminution of vision, complaining of annoyinghalos of light around objects withsubsequent reduction in visual performances. In addition, we think that the SFD is a potential type of retinal phototoxicity that could be attributed toexcessive exposure to blue light emitting LEDs, encountered in the manufacture of modern digitalscreens and electronic devices,with subsequentphotochemical injury [3-5, 9-12]. Furthermore, we have discovered that SFD is a temporary retinal phototoxicity phenomenon that has short-term adverse impacts on normal foveal functions and intact macular integrity. Moreover, SFDmight be reversed by restrict reduction of the screen-timethus minimizing the retinal exposure to blue light emitting screens [9-12]. Meanwhile, we unfortunately don't know underlying pathophysiological mechanisms ofSFD; however, it might becould be caused bythe macular cone/bipolar cell dysfunction due to the cone adaptation and/or saturationresulting fromtheexcessive levels of blue light with a potential level of retinal phototoxicity resulting in a photochemical injury inducing SFD.Strict reduction or cessation of exposure to blue light for4 weeks results in spontaneous resolution of cone adaptation/saturation thuseventually the retina regains its normalfoveal functions and responses withnormal visual acuities and performances.

Similar to our outcomes,Cougnard-Gregoireet al. [14] concluded that the potential toxicity of long-term cumulative exposure to blue light emitting LEDs and the dose-response effect are

currently unknown.In agreement with our results, Li et al [22] reported the mfERG outcomes that ≥8daily hours viewing of the screensreduced the retinal photoreceptor cells amplitude in the parafoveal region of the maculawith delayed peak time. They alsostated thatthe long-term exposure toblue light is a cause of structural and functional damage of the retinal tissue [22].

Finally, our studies recommended that the higher educational authorities should re-plan the mandated computer system use program and consider other alternatives. We also recommend that further future studies including mfERG investigations regarding this topic.

Ethics Statements

The three studies by Iqbal et al. gained the approval of the Medical Research Ethics Committee (MREC) in Faculty of Medicine, Sohag University, Egypt. All three studies were registered as clinical trials at the ClinicalTrial.gov (ID:NCT04398212 and NCT04405648) and the Pan African Clinical Trial Registry (PACTR201811618954630). All studies were conducted in accordance with the tenets of the Declaration of Helsinki.All participants signed an informed consent prior to enrolment in the studies.

Supplementary material and/or additional information

None.

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