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ORIGINAL RESEARCH

Objective Evaluation of Relationship Between Tear Film Stability and Visual Fatigue

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Purpose: To investigate the relationship between tear film stability and visual fatigue using two objective measurements: the non-invasive tear film break-up time (NI-BUT) and the binocular fusion maintenance (BFM) test.

Methods: Eleven young adult volunteers (age [mean ± standard deviation], 20.7 ± 1.4 years) participated in this study. The NI-BUT was determined using the distortion of the mire ring. BFM was assessed by measuring the transmittance of liquid crystals placed in front of the subject's non-dominant eye when binocular fusion was broken, and non-dominant eye was shifted to heterophoric. The volunteers were administered the NI-BUT and BFM before and after a 30-minute visual task.

Results: NI-BUT (pre vs post: 9.12 ± 1.00 s vs 5.69 ± 3.11 s) was significantly shorter in the post-visual task than in the pre-visual task ($P = 0.011$). BFM (0.95 ± 0.09 vs 0.75 ± 0.16) was significantly lower in the post-visual task than in the pre-visual task ($P = 0.012$). The change in NI-BUT was significantly and positively correlated with the change in BFM ($R^2 = 0.385$, $P = 0.042$).

Conclusion: These objective findings support the association between tear film stability and visual fatigue.

Plain Language Summary: Although subjective questionnaire studies have reported that eye dryness is associated with increased eye fatigue, objective evidence remains insufficient. In this study, we investigated the relationship between eye dryness and eye fatigue using objective measurements and found a correlation between them. These findings strengthen previous research and suggest the importance of preventing eye fatigue by maintaining proper tear film stability.

Keywords: eye movements, binocular fusion, binocular vision, tear film, visual fatigue

Introduction

The proliferation of digital devices in modern society has led to an increasing prevalence of computer vision syndrome (CVS), also known as digital eye strain (DES).[1,2] CVS manifests as a constellation of vision-related physical and mental symptoms that develop in response to prolonged digital device usage, particularly in occupational settings.[3] The primary manifestations include visual fatigue, dry eyes, headache, blurred vision, and musculoskeletal discomfort in the neck and shoulder regions.[3,4] Recent meta-analytic findings indicate that approximately 66% of digital device users experience some form of CVS symptoms.[5]

The ubiquity of smartphones, characterized by their convenient internet accessibility,[6] has become particularly noteworthy, with studies indicating that over 50% of young people across Asia,[7,8] the United States,[9] and Europe[10] engage in daily social networking activities via these devices. While smartphones have revolutionized modern communication patterns and become integral to contemporary life, their widespread adoption has been accompanied by various health concerns,[11] including acute acquired esotropia,[12] dry eye disease,[13] and visual fatigue.[14]

Previous research has established that more than 30% of patients with dry eye disease report concurrent visual fatigue,[15–17] suggesting a potential relationship between tear film stability and visual fatigue. However, the existing literature has

predominantly relied on subjective questionnaire-based assessments, resulting in a paucity of objective evidence. The development of objective methodologies to evaluate this relationship would provide more robust support for this association.

Traditional understanding has linked visual fatigue primarily to vergence and accommodation parameters,[18,19] which are not directly associated with tear film stability and may be influenced by aging processes. However, common symptoms reported by individuals experiencing visual fatigue, such as blurred vision and diplopia, may be attributed to tear film instability. Recent technological advances have enabled the assessment of binocular fusion maintenance (BFM) through focus on binocular fusion,[20–23] particularly relevant given that patients reporting diplopia and blurred vision frequently experience visual fatigue. Current evidence suggests that BFM may serve as a quantitative indicator of visual fatigue.

Based on these observations, we hypothesize that investigating the correlation between BFM and tear film stability could provide an objective, quantitative assessment of the relationship between tear film stability and visual fatigue. This approach may offer new insights into the mechanisms underlying digital eye strain and inform more effective interventions for this increasingly prevalent condition.

Methods

Subjects

A total of 11 young adult volunteers (age [mean ± standard deviation], 20.7 ± 1.4 years) participated in this study. All subjects underwent complete ophthalmologic examinations, including the determination of ocular dominance using the hole-in-the-card test, assessment of best-corrected visual acuity at a distance (5.0 m), near the point of convergence, evaluation of stereoscopic acuity at 40 cm (Titmus Stereo test; Stereo Optical Co., Inc., Chicago, IL, USA), assessment of heterophoria using the alternating cover test at near (33 cm), and far (5.0 m) distance assessments, and examinations of the fundus. Stereoacuity was converted to the logarithm of the arcsec (log arcsec).

Participants in this study were enrolled between May 1, 2023, and September 31, 2023. After explaining the nature of the study and possible complications, all subjects provided informed consent. This study adhered to the Declaration of Helsinki of the World Medical Association. The Institutional Review Board of Teikyo University approved the experimental protocol and consent procedures (approval no. 19–224-3).

Binocular Fusion Maintenance

BFM can be assessed by reducing the intensity of the incident light on one eye, which is defined by the number of photons, because the perceptive size of the retinal image depends on the intensity of the incident light.[24]

In this study, we used a custom-made system to measure the BFM (Figure 1 and Video S1). This system consisted of spectacle-type video-oculography (VOG) (Pupil Core, Pupil Labs, Berlin, Germany), a liquid crystal shutter (LCS) (Large Liquid Crystal Light Valve - Controllable Shutter Glass, Adafruit, New York, NY, USA), and a starburst target at 33 cm. The LCS could arbitrarily change the transmittance from 0.7% to 34.1% relative to the voltage sent from the microcomputer (Arduino Uno, Arduino, Turin, Italy).

The participants continued to fixate on the starburst target through the LCS, and both eye positions were recorded continuously for 34s (Movie 1). The transmittance of the LCS in the non-dominant eye, which was determined by the hole-in-the-card test, was set at 34.1% for 3s and was then reduced sequentially by 1.66% every second. Between 23 and 28s, the transmittance was maintained at 0.7%; thereafter, it increased and remained at 34.1% between 28 and 34s. The transmittance for the dominant eye was sustained at 34.1% throughout the 34s period. The BFM test evaluated the intensity of the incident light ratio in both eyes during the binocular fusion break and was conducted three times before the visual task and three times after the visual task.

The eye positions and pupil diameters in both eyes were exported to a comma-separated values file. Data were excluded when the pupil diameter changed by >2 mm between consecutive frames because of blinking, and the missing values were replaced with a linearly interpolated value calculated from an algorithm written in Python 3.11.1. The BFM analysis followed the procedure of Hirota et al.[20] The BFM was calculated using the following equation:
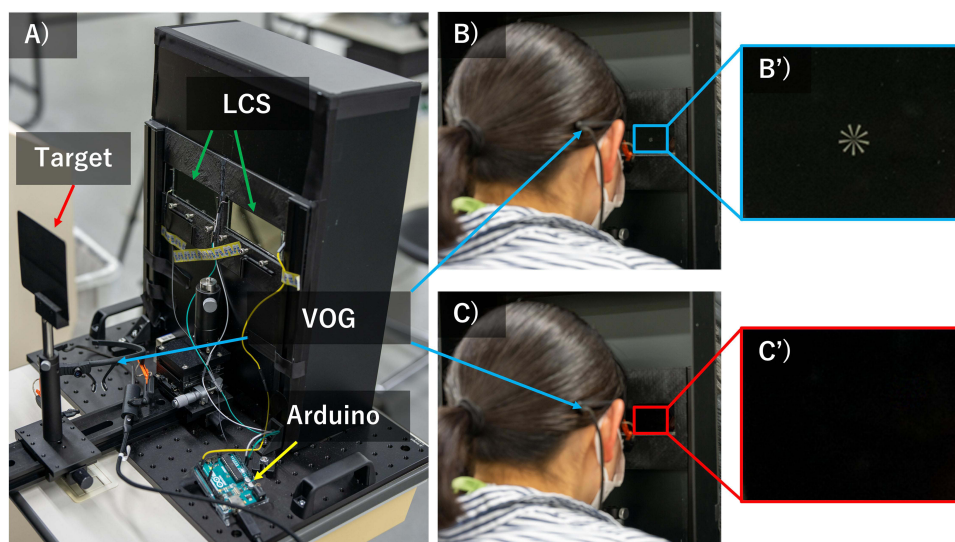
Figure 1 BFM system. The BFM system included a VOG system that recorded the participant's eye position, an LCS, an Arduino that controlled the LCS, and the fixation target. The VOG system and Arduino were connected to a personal computer and synchronized (**A**). The participants wearing the VOG device fixated on the target, which was placed 33 cm in front of their eyes, via the LCS (**B** and **C**). The transmittance of the LCS was set at 34.1% for 2 s and then reduced sequentially by 1.66% every second (**B'** and **C'**).
Abbreviations: BFM, binocular fusion maintenance; LCS, liquid crystal shutter; VOG, video oculography.

$$Binocular\ Fusion\ Maintenance\ (BFM) = 1 - \frac{Transmitance\ (nondominant\ eye)\ at\ binocular\ fusion\ break}{Transmitance\ (dominant\ eye)}$$

In this study, the change in BFM was defined as the difference between the post-BFM and pre-BFM values.

Non-Invasive Tear Film Break-Up Time

Tear film instability is one of common symptoms in CVS.[3,4] In this study, non-invasive tear film break-up time (NI-BUT) was measured using RT-7000 (Tomey Corp., Aichi, Japan) with a tear stability analysis system (TSAS),[25] which irradiates the anterior eye using infrared light, and 15 mire rings from the blue-lighted cone were projected onto the corneal surface. The anterior eye images were captured every second for 10s. The participants were instructed to refrain from blinking as long as possible and to look at the central target during the measurement. The examiner began the measurements after blinking.

In the NI-BUT analysis, each of the 15 mire rings was decomposed into 256 individual data points, resulting in a total of 3840 measurement points (15 mire rings × 256 data points) were obtained. The TSAS compares the brightness of the mire rings with the initial brightness at 0 s. If the brightness decreased below a predefined threshold (ring breakup levels were set to 0.010 and 20.00), the computer recorded the point at which the threshold crossed the tear film BUT, ie, the NI-BUT. The NI-BUT was measured in the participants' right eye before and once after the visual task. Participants were excluded if their NI-BUT was less than 5 s before the visual task.

In this study, the change in NI-BUT was defined as the difference between the post-NI-BUT and pre-NI-BUT values.

Visual Task

In this study, we used an iPod Touch to simulate smartphone use. The participants played Mario Kart Tour (Nintendo Co., Ltd., Kyoto, Japan) as the visual task. The participants played the game under fully corrected vision for 30 min. The visual distance between the participant's eyes and the smartphone display was set at 20 cm using a neck strap (Figure 2), which aligns with an earlier study indicating that 20 cm is the average smartphone viewing distance in a sitting position.[26]

Statistical Analysis

Differences in NI-BUT and BFM between the pre- and post-visual tasks were analyzed using the Wilcoxon signed-rank test.

Figure 2 Visual task. Participants played a smartphone game for 30 min under wearing spectacle-type VOG. The visual distance between the participant's eye and smartphone display was set at 20 cm by using a neck strap.
Abbreviation: VOG, video-oculography.

The relationship between the changes in NI-BUT and BFM was evaluated using Pearson's correlation coefficient and single linear regression analysis.

The repeatability of the BFM test was analyzed using Bland-Altman analysis.[27,28] Data were randomly extracted for two of the three measurements during the pre-visual task.

SPSS version 26 (IBM Corp., Armonk, NY, USA) was used to determine the significance of the differences, and $P < 0.05$ was considered statistically significant.

Results

Table 1 presents the participants' characteristics. The mean ± standard deviation of the refractive errors (spherical equivalents) of the dominant eye was −1.72 ± 3.15 D, and that of the non-dominant eye was −2.08 ± 3.11 D. The best-corrected visual

Table 1 Characteristics of Volunteers

ID	Age	Gender	Spherical Equivalent (D)		Ocular Deviation (PD)		Stereo Acuity (log arcsec)
			RE	**LE**	**Near**	**Distant**	
1	19	F	−2	−1.875	−4	−6	1.60
2	19	F	0	0.25	−4	−8	1.60
3	19	M	−2	−3.625	−6	−2	1.60
4	22	F	0.25	−2.125	−4	−4	1.70
5	21	F	−0.625	0.5	−4	−2	1.60
6	20	F	−0.25	−0.375	−6	−2	1.60
7	20	F	−5	−5.5	−4	−4	1.60
8	23	M	−6.875	−6.875	−8	−2	1.60
9	21	F	−2.375	−2.375	−4	−8	1.60
10	21	M	5.25	4.5	−4	0	1.60
11	23	M	−5.25	−5.375	0	−2	1.60

Note: The ocular deviations of minus and plus signs indicate exodeviation and esodeviation, respectively.
Abbreviations: F, female; M, male; RE, right eye; LE, left eye; D, diopter; PD, prism diopter.

acuity was 0.0 logMAR units or better in all subjects. The average heterophoria was -4.7 ± 1.9 prism diopters (PDs) at a distance and -3.6 ± 2.5 PDs up close. All healthy volunteers had a stereoacuity of 40.9 ± 2.9 log arcsec (range: 40–50 s).

The NI-BUT (9.12 ± 1.00 s vs 5.69 ± 3.11 s) was significantly shorter in the post-visual task than in the pre-visual task ($P = 0.011$) (Figure 3). The BFM (pre vs post: 0.95 ± 0.09 vs 0.75 ± 0.16) was significantly lower in the post-visual task than in the pre-visual task ($P = 0.012$) (Figure 4).

The change in BFM (-0.20 ± 0.18) was significantly and positively correlated with the change in NI-BUT (-3.43 ± 3.19 s) ($R = 0.621$, $R^2 = 0.385$, $P = 0.042$) (Figure 5).

The BFM between single measurements did not significantly differ (first and second measurements, 0.961 ± 0.085; and 0.968 ± 0.079; $P = 0.157$, respectively). The mean value of the differences between the two measurements was -0.007 ± 0.017, and the correlation between the two measurements was not significant ($R^2 = 0.103$, $P = 0.27$). The 95% limit of agreement (LoA) ranged from 0.041 to 0.027.
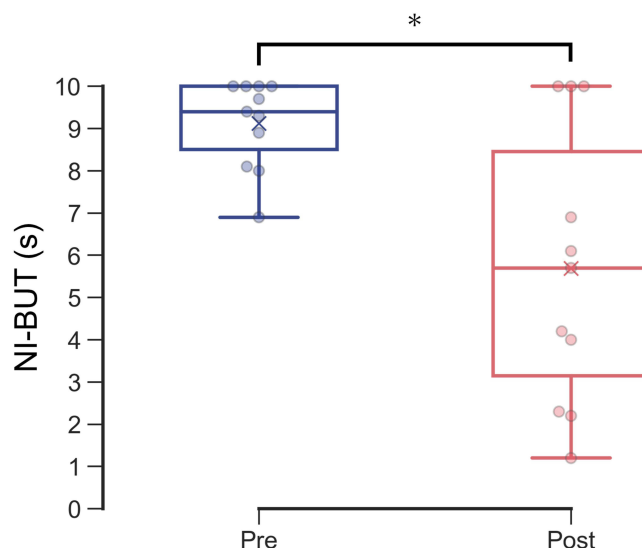

Figure 3 Change in NI-BUT between pre- and post-visual tasks. The blue and red box plots with dots indicate the NI-BUT in the pre- and post-visual tasks. The blue and red crosses indicate mean values. The NI-BUT score was significantly lower in the post-visual task group than in the pre-visual task group. * $P = 0.011$, Wilcoxon signed-rank test.
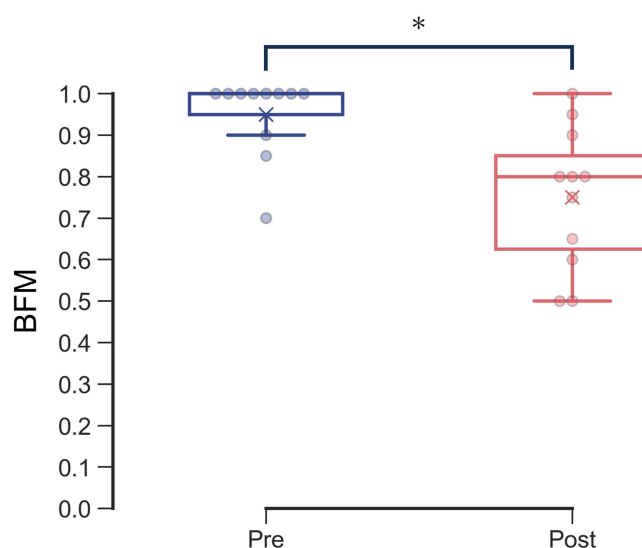**Abbreviations**: NI-BUT, non-invasive tear film break-up time; Pre, pre-visual task; Post, post-visual task.

Figure 4 Change in BFM between pre- and post-visual tasks. The blue and red box plots with dots indicate the BFM in the pre- and post-visual tasks. The BFM was significantly lower in the post-visual task than in the pre-visual task. * $P = 0.012$, Wilcoxon signed-rank test.
Abbreviations: BFM, binocular fusion maintenance; Pre, pre-visual task; Post, post-visual task.
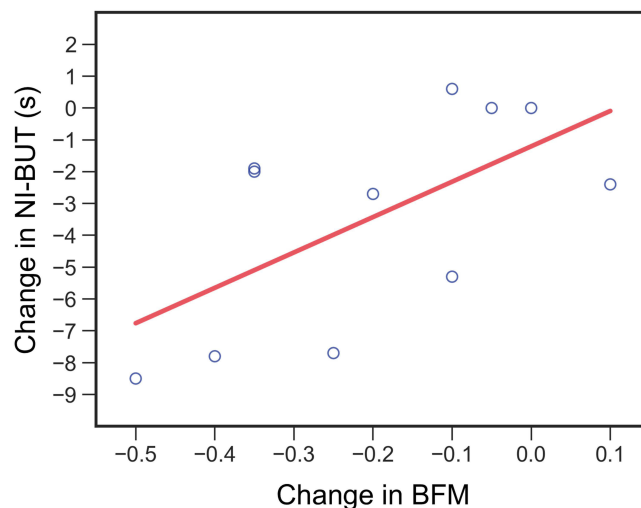
Figure 5 Relationship between changes in NI-BUT and BFM. The red lines indicate the regression lines. The change in BFM significantly correlated with the changes in the NI-BUT ($R = 0.621$, $R^2 = 0.385$, $P = 0.042$). Regression line: $11.114x - 1.204$.
Abbreviations: BFM, binocular fusion maintenance; NI-BUT, non-invasive tear film break-up time.

Discussion

In this study, we investigated the relationship between tear film stability and visual fatigue using objective method of NI-BUT and BFM. The NI-BUT and BFM were significantly lower in the post-visual task than in the pre-visual task (Figures 3 and 4). Furthermore, the change in NI-BUT was significantly and positively correlated with the change in BFM (Figure 5). These findings suggest that, even from objective measurements, there is association between tear film stability and visual fatigue.

Moreover, our findings suggest that digital device use may induce visual fatigue, subsequently leading to decreased tear film stability. While transient visual fatigue can resolve with adequate rest periods, chronic reduction in tear film stability may contribute to the development of dry eye disease.[29] In such cases, patients may experience increased visual stress even in the absence of digital device viewing. This may explain why patients with dry eye disease frequently report visual fatigue during routine activities.

The temporal dynamics of tear film stability during prolonged visual tasks warrant careful consideration. Hirota et al showed that during a 60-minute visual task, participants exhibited a high frequency of incomplete blinks during the initial 30 minutes, accompanied by a decrease in tear film stability as measured using NI-BUT by TSAS.[30] Our findings align with these observations, showing a significant reduction in NI-BUT following a 30-minute visual task. This consistency across studies suggests a reproducible pattern of tear film degradation during sustained visual task.

Our findings showed that BFM was significantly lower following the visual task compared to baseline measurements (Figure 4). These findings align with those reported by Hirota et al[20] who examined the relationship between subjective visual fatigue, assessed through questionnaires, and objective measurements using BFM. Their investigation reported that symptoms such as blurred vision and diplopia were frequently noted during experiences of visual fatigue, and these symptoms may be associated with decreased BFM. Moreover, the repeatability of the BFM test in this study (mean: −0.007, LoA: −0.041 to 0.027) was similar to that of a previous study (mean: 0.000, LoA: −0.111 to 0.111).[20] These findings suggest that the BFM test is useful in evaluating visual fatigue.

A significant positive correlation was observed between NI-BUT and BFM measurements (Figure 5). This relationship suggests a connection between tear film stability and visual function: tear film instability increases higher-order aberrations, resulting in degradation of retinal image quality.[31–33] The reduction in tear film stability may cause an imbalance in retinal images between the left and right eyes, potentially increasing the load on binocular fusion and leading to decreased BFM. These changes may contribute to visual fatigue. However, the R^2-value between NI-BUT and BFM was low. These results suggest that tear film instability is one of the factors that induces visual fatigue, and other factors are involved in visual fatigue, such as vergence[34–36] and accommodation.[37,38] Therefore, the parameter of tear film stability alone may be insufficient to model visual fatigue, and it may be necessary to evaluate tear film stability, vergence, and accommodation simultaneously.

In this study, we observed a relationship between tear film stability and visual fatigue. Although our findings enhance the hypothesis that the reduction in tear film stability leads to visual fatigue, we were unable to quantify the extent of visual fatigue specifically attributable to reduced tear film stability. Previously, Hirota et al observed an interesting phenomenon in their 60-minute protocol: after the 30-minute mark, participants showed an increase in complete blink frequency, which corresponded with a temporary improvement in tear film stability.[30] While our study was limited to a 30-minute duration due to the additional time required for BFM measurements (approximately 5 minutes), future investigations examine the relationship between tear film stability and BFM at extended time points, particularly around the 45-minutes.

Conclusions

Objective measurements revealed that both NI-BUT and BFM significantly decreased after the visual task compared to baseline measurements. Moreover, we found a significant positive correlation between the changes in NI-BUT and BFM. These objective findings support the association between tear film stability and visual fatigue.

Data Sharing Statement

The data of this study have been uploaded to zenodo (doi: 10.5281/zenodo.10039342) after removing personal information, and are available to anyone.

Ethics Approval and Informed Consent

This study adhered to the Declaration of Helsinki of the World Medical Association. The Institutional Review Board of Teikyo University approved the experimental protocol and consent procedures (approval no. 19–224-3).

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Author Contributions

All authors made significant contributions to the work reported, in the conception, study design, execution, acquisition of data, analysis and interpretation. They drafted, revised and critically reviewed the article; approved the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Disclosure

M.H. reports patents WO2017159225 and US10959615 licensed to Topcon Corp. The authors report no other conflicts of interest in this work.

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