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ORIGINAL ARTICLE

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Is critical flicker-fusion frequency a valid measure of visual fatigue? A post-hoc analysis of a double-masked randomised controlled trial

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Abstract

Purpose: Critical flicker-fusion frequency (CFF) has been used in clinical studies as a measure of visual fatigue. We examine the correlation between CFF and subjective reports of visual fatigue in a group of symptomatic computer users, to consider whether CFF may be used as a surrogate measure of visual fatigue symptoms.
Methods: We analysed data from a previous randomised controlled trial. One hundred and twenty adults, diagnosed with computer vision syndrome, had CFF and visual fatigue symptoms quantified before and after a visually demanding 2-h computer task. Symptoms were assessed using a questionnaire with nine subcomponents that summed to a total score of 900. CFF was measured using a two-interval forced-choice method, with the flicker rate altered by a computer-controlled staircase procedure. For our primary analysis, we determined Spearman correlation coefficients between post-task symptom scores and CFF, and between change from baseline symptom scores and CFF. We also used a bootstrap procedure to consider whether symptom score subcomponents were significantly (Bonferroni-corrected) different from overall scores with regard to their correlations with CFF.
Results: Although visual fatigue symptom scores altered significantly post-task (mean change: 92 units; 95% confidence interval [CI]: 11 to 122), CFF did not (mean change −0.7 Hz; 95% CI: −1.7 to 0.3). There was no significant correlation between overall symptom scores and CFF, either for the post-task ($r = -0.13$; 95% CI: −0.31 to 0.05) or the change from baseline ($r = -0.18$; 95% CI: −0.35 to 0.01) analysis. Subcomponents of the symptom questionnaire did not show a significant correlation with CFF, either for the post-task or the change from baseline analysis.
Conclusions: We find that CFF is not a useful surrogate for symptoms of visual fatigue, given its low correlation with scores on a visual fatigue symptom questionnaire.

KEYWORDS
asthenopia, computer vision syndrome, critical flicker-fusion frequency, digital eye strain, eye strain, visual fatigue

INTRODUCTION

Computer use is ubiquitous in contemporary society. An estimated 65%–90% of computer users report eye strain associated with this task, often referred to as 'computer vision syndrome' (CVS) or 'digital eye strain'.[1] In addition to eye strain, other common ocular symptoms associated with CVS are blurred vision, dry eyes and ocular redness; these can occur immediately or after several hours of computer use.[2] In the literature, the spectrum of symptoms associated with CVS has been defined using different terminologies, including eye strain,[3] visual fatigue[4–6] and asthenopia.[7] For the purpose of this study, we use the phrase 'visual fatigue' to define the ocular symptoms associated with CVS.

With CVS affecting an estimated 60 million people worldwide,[8] a range of interventions have been investigated for this highly prevalent condition.[2,9,10] The most common approach used to diagnose CVS involves patient questionnaires to quantify symptomatology. A widely adopted questionnaire was developed and validated by Segui et al.,[11] which captures 16 distinct symptoms (with respect to both frequency and intensity) associated with computer use; a score of six or more out of 32 is used to identify individuals with CVS. There is interest in using alternative methods to quantify CVS that do not require individuals to rate their symptoms. Some such approaches include critical flicker-fusion frequency (CFF),[12,13] near point of accommodation,[14] near point of convergence,[14] and saccadic eye movements.[15] In this regard, CFF, defined as the frequency at which a flickering light appears continuous to an observer, has received substantial attention, including its adoption in randomised controlled trials (RCTs) evaluating CVS treatments.[13,16–23] Theories about where in the visual system this frequency limit is set include both retinal and cortical loci.[24] The idea that the CFF reflects cortical functioning has presumably been influential in its selection for studies exploring its relationship to factors such as intelligence,[25] psychotropic drug use[26] and fatigue,[27] including fatigue when using visual display terminals.[28] A decrease in CFF has been suggested to be an indicator of visual fatigue.[13] More recently, comparisons of psychophysical and electrophysiological recordings suggest that the limit of CFF is due to precortical filtering, at least for achromatic flicker.[29]

At present, there is uncertainty regarding the relationship between CFF and visual fatigue symptoms. If CVS symptoms highly correlate with CFF, then it might be appropriate to use CFF as a surrogate measure of symptom scores in clinical studies, including those exploring drug therapies for CVS. To date, only one study[30] has specifically investigated the association between visual fatigue symptoms in CVS and CFF, and found no significant correlation between these measures. However, the sample size for this study was modest ($N = 30$), which may have limited the ability to find a relationship. Furthermore, the study used a criterion-dependent measure of CFF, as have many other studies using CFF to measure visual fatigue.[3–5,12,13,31–33] Criterion-dependent measures—such as the method of limits—yield thresholds that depend upon a person's willingness to indicate that a light is flickering. For example, an observer may return a lower CFF if they only respond when they are certain that flicker is present, in contrast to a higher CFF if they respond to even a vague suggestion of flicker. As a result, a change in CFF measurement may not necessarily reflect a change in the temporal response of the visual system but rather could reflect a change in an observer's willingness to respond (i.e., their *response criterion*). Although methods can be used to quantify biases due to response criterion, previous studies did not adopt such approaches.[3–5,12,13,31–33] A review of 33 studies examining CFF and psychotropic drugs similarly found that all failed to quantify bias,[26] suggesting this is a common limitation among studies measuring CFF. An alternative to quantifying the influence of response criterion is to use forced-choice methodologies, which eliminate this potential methodological bias by forcing observers to indicate which of two stimuli is flickering, rather than whether or not a single stimulus is flickering.

In the present study, we performed a post-hoc analysis of data derived from a double-masked RCT that measured CFF thresholds using a criterion-free method, as well as CVS symptoms, for a generous sample size ($N = 120$). This allowed us to test a hypothesis that the CFF strongly correlates with CVS symptoms, and thus has utility as a surrogate marker for visual fatigue symptomatology.

Key points

- Critical flicker-fusion frequency (CFF) is not meaningfully correlated with subjective symptoms of computer vision syndrome (CVS) and so should not be used as a surrogate for subjective questionnaires of visual fatigue.
- Unlike the present study, previous randomised controlled trials on CVS used CFF measures that were potentially influenced by shifts in participants' willingness to report that flicker was seen.
- Although historically argued to represent a cortical processing limit, the modern literature suggests that achromatic CFF is limited by precortical processing.

METHODS

Study overview

This was a post-hoc analysis of a four-arm, single-centre, double-masked RCT that investigated the efficacy of blue light-blocking spectacle lenses, relative to placebo, for alleviating signs and symptoms of eye strain with computer use.[20] This RCT also investigated the role of clinician advocacy (i.e., the intervention either was, or was not, advocated for by the clinician) in modulating the study outcomes. A total of 120 participants were randomised (30 in each allocation arm) and completed the study.

The RCT was conducted in accordance with the tenets of the Declaration of Helsinki and ethical approval was granted by The University of Melbourne Human Research

Ethics Committee (ID #1852643). The post-hoc analysis described in the current study focussed on assessing the association between subjectively reported symptoms of visual fatigue and the CFF.

Participants

Symptomatic computer users, verified using a validated questionnaire[11] (CVS-Q, ≥6), aged 18–40 years were eligible to participate in the RCT. Participants were also required to have unaided or contact lens-corrected binocular near vision of at least N8 at 40 cm. Exclusion criteria were a history of neurological disease, migraine or nystagmus by self-report and individuals who were optometry students or eye care practitioners.

Study design

A detailed description of the study design, interventions, study procedures, masking techniques and outcome measures have been previously published.[20] In brief, following an initial baseline screening, participants were randomised (1:1:1:1) to one of four study arms, representing all possible combinations of spectacle intervention/advocacy interventions (blue light-blocking vs. non-blue light-blocking) and clinician advocacy (clinician did/did not advocate for the efficacy of the intervention). Though the study included a placebo arm (non-blue light-blocking lens), all participants were led to believe they were assigned to the active intervention arm (blue light-blocking lens). The term 'blue light-blocking' was not mentioned in any of the publically available study documents, to discourage potential participants from researching the topic in advance. The active lens arm group received Essilor Prevencia blue light-blocking lenses (Essilor.com), and the control placebo arm group received clear lenses (Essilor Crizal UV, Essilor.com) with a conventional anti-reflection coating. Lenses in both study arms were plano (0 D). Following baseline measures, participants were provided with their assigned intervention and then completed a visually demanding 2-h, data-focussed computer task. The set of outcome measures included both direct (visual fatigue questionnaire score) and indirect measures (CFF, near point of accommodation, near point of convergence, saccadic eye movements and blink rate) of visual fatigue, which were performed both pre- and post-computer task.

Outcomes

The main outcome of the present analysis was the association between overall subjective reported symptoms of visual fatigue and CFF. The level of subjective visual fatigue was quantified with a questionnaire[6] comprising nine symptom domains (eye pain, eye strain, blurred vision, irritation, double vision, burning sensation, dry eye, tearing and headache). Each participant was asked to rate their symptom level in each of these domains on a visual analogue scale (from 0 = none to 100 = intense); a total symptom score was calculated by summating all nine domains (maximum score = 900). In addition, the association between CFF and each of the nine domains of the visual fatigue symptom scores was analysed.

Critical flicker-fusion frequency was measured using a two-interleaved, two-interval forced-choice staircase procedure (2-up, 1-down) for a green light emitting diode subtending 2°, presented in a dimly illuminated room. The stimulus in one interval was at fixed high frequency (100 Hz; i.e., well above CFF), and thus would always appear continuous to an observer. Within each staircase, the stimulus in the other interval was initially presented at 25 Hz and then altered with a step size of 5 Hz until two reversals were reached, and then further altered in a step size of 1 Hz. The order of the stimuli was randomised, and each target was presented for 0.50 s; the diode was off during nonstimulus times. The interval between the two stimulus presentations was 0.25 s, which—given the diode returned to the off state during this time—provided a clear distinction between the two intervals. Participants were instructed to indicate which one of the two stimuli was flickering by an appropriate key press. Testing was considered complete at the end of four reversals in each staircase. CFF was calculated as the average of the last two reversals in each staircase.

Statistical analysis

For the current analysis focusing on the relationship between subjective visual fatigue and CFF, data across the four RCT intervention arms were combined. This approach was considered appropriate given that the original study found no intervention effects (with respect to either the type of spectacle or advocacy). Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, ibm.com) or R (version 3.3.0; r-project.org). Although not part of the prespecified analysis protocol of the original clinical trial, the statistical analyses in the current paper were defined a priori. For the primary analysis, a p value < 0.05 defined statistical significance.

Data normality was assessed using the Shapiro–Wilk test. Within-study groups (i.e., pre- vs. post-computer task) analysis was performed using a paired t-test or Wilcoxon test (as appropriate), to determine whether subjective symptoms and/or CFF changed after performing the computer task. For the primary analyses, the correlation between post-task overall visual fatigue score (out of 900) and post-task CFF was assessed using the Spearman correlation. Likewise, the relationship between the change from baseline (i.e., the difference between pre- vs. post-task values) in the overall visual fatigue score and the change from baseline in CFF was assessed using Spearman correlation.

In addition, both the change from baseline and post-task CFF measures were correlated with each of the nine domains of the visual fatigue symptom scores to assess whether CFF was more associated with a specific symptom domain. We determined confidence intervals (CIs) around the correlation coefficients using a nonparametric bootstrap procedure (*N* = 10,000 replicates). Bootstrapping was used as, unlike with traditional inferential statistics, this approach does not make assumptions regarding the distribution of data and does not require null hypothesis testing.[34] For this analysis, we used 99.4% CIs, as determined by a Bonferroni correction (CI width = 100%–5%/9), to adjust for the multiple comparisons performed and to maintain a Type II error rate of 5%. For all analyses, a correlation was deemed significant if its CI did not include zero.

RESULTS

Comparison of the post-computer task visual fatigue scores and the baseline [=pre-computer task] visual fatigue scores was statistically significant (120 participants; median difference: 50 units; 96.5% CI: 36 to 99; $p < 0.001$), indicating participants' overall visual fatigue levels had increased at the end of the 2-h computer task. However, there was no significant difference, pre- versus post-computer task, for the CFF outcome (120 participants; mean difference: −0.7 Hz; 95% CI: −1.6 to 0.3; $p = 0.15$).

The correlation analyses between: (i) change (from baseline) in overall visual fatigue score and change in CFF and (ii) post-task overall visual fatigue score and post-task CFF, each showed no significant association (Table 1 and Figure 1). The bootstrapping analysis, to compare the relationship between CFF and each of the nine visual fatigue symptom domains, also showed no significant association for both the change from baseline and the post-task measures (Table 2).

DISCUSSION

In the current analysis of a doubled-masked RCT, there was no statistically significant correlation between CFF and the overall visual fatigue questionnaire score, for either the change from baseline or endpoint measures, among a population of adult symptomatic computer users. Our exploratory analysis also found no significant correlations between CFF and the individual questionnaire items (symptom domains) comprising the visual fatigue questionnaire. The magnitude of all of our correlation coefficients might be classified as 'weak' within psychological research,[35] indicating that CFF is poorly related to visual fatigue scores and so should not be used as a replacement for visual fatigue questionnaire scores.

Although CFF has been used as a measure of visual fatigue in many studies,[3–5,31,32] to date, only one study has investigated the association between CFF and subjective symptom scores. Yan and Rosenfield[30] recruited 30 participants, who performed a reading task across two different sessions for 20 min, using a tablet computer or children's reading book. Although their task induced a significant increase in CVS symptoms, they found a lack of correlation between overall symptom scores and CFF ($R^2 = 0.10$; $p = 0.08$). In their study, participants were not randomised to the session condition, both participant and outcome assessor were not described as being masked to the interventions and the authors did not specifically recruit symptomatic computer users despite such people being the most likely to benefit from an objective measure for diagnosing visual fatigue. As previously noted, this study[30] also used a criterion-dependent measure of CFF, where

TABLE 1 Correlations between CFF and overall visual fatigue scores

Measure	*r*	*p* Value	95% CI
Post-task	−0.132	0.15	−0.309 to 0.053
Change from baseline	−0.177	0.05	−0.350 to 0.008

Abbreviations: CI, confidence interval; *r*, correlation coefficient.

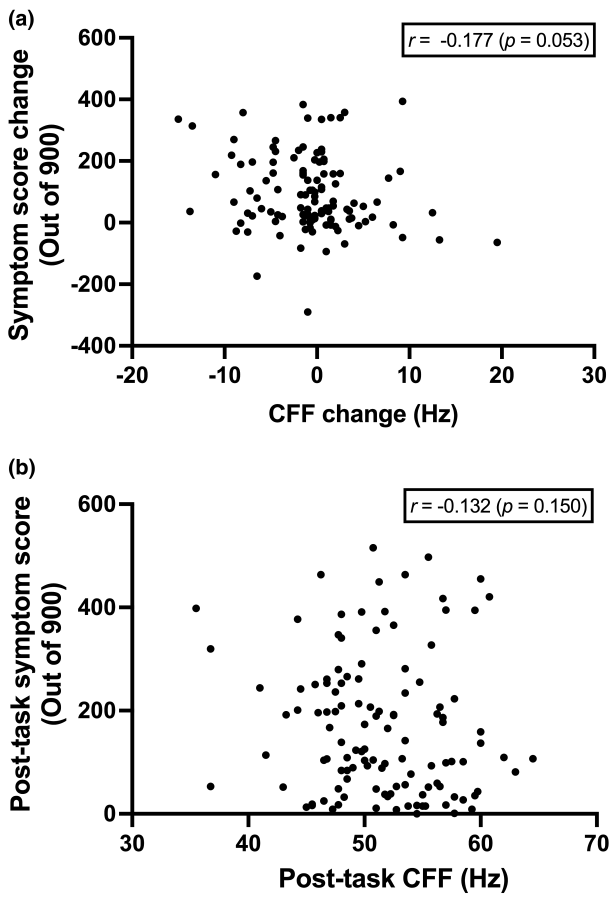

FIGURE 1 Spearman correlation (*ρ*) between critical flicker-fusion frequency (CFF) and overall visual fatigue symptom scores (out of 900) for change from baseline (a) and post-2-h computer task time points (b).

TABLE 2 Correlations between critical flicker-fusion frequency and visual fatigue questionnaire subdomains

	Post-task measure		Change from baseline measure	
Questionnaire item	**Spearman correlation, median**	**99.4% CI**	**Spearman correlation, median**	**99.4% CI**
Eye pain	−0.009	−0.175 to 0.169	−0.001	−0.211 to 0.205
Eye strain	0.045	−0.086 to 0.178	0.022	−0.133 to 0.167
Blurred vision	0.138	−0.080 to 0.367	0.145	−0.102 to 0.393
Irritation	0.063	−0.091 to 0.222	−0.057	−0.253 to 0.126
Double vision	−0.025	−0.276 to 0.230	0.127	−0.093 to 0.373
Burning sensation	0.002	−0.179 to 0.203	0.045	−0.156 to 0.258
Dry eye	0.062	−0.139 to 0.283	−0.058	−0.217 to 0.103
Tearing	0.040	−0.228 to 0.328	0.226	−0.026 to 0.486
Headache	−0.076	−0.285 to 0.150	0.061	−0.204 to 0.348

Abbreviation: CI, confidence interval.

changes in CFF could represent a change in response criterion rather than a change in temporal resolving capability. The current study allowed all of these potential limitations to be addressed. Using a four-fold larger sample size, our findings broadly align with those of Yan and Rosenfield,[30] whereby CFF was found to not be significantly associated with overall visual fatigue scores. The present analyses also found no significant relationship between CFF and individual visual fatigue symptoms in CVS.

Whilst our findings suggest that CFF should not be used as a surrogate measure for CVS visual fatigue symptoms, it is also relevant to consider whether CFF is useful as a standalone parameter relevant to CVS. After subjective symptom scores, CFF is the most used outcome measure for assessing eye strain in RCTs of CVS interventions.[13,17–23,36] In itself, frequent use of CFF as a parameter does not necessarily justify its appropriateness as an outcome measure. In studies that have used CFF to measure the efficacy of CVS interventions, the magnitude of change in this parameter has been 2 Hz or less.[37] It is unclear whether this small change is related to the poor efficacy of the interventions or whether CFF is an unsuitable measure of visual fatigue. The minimal clinically important difference in CFF is not clear, yet clinical studies investigating interventions—including those for CVS—ideally should specify what changes are considered clinically important. A further consideration in determining what changes in CFF are meaningful is that the variability associated with CFF measures using a method of limits can be affected by response bias.[38] If such biases move in concert with general fatigue (i.e., a fatigued person also has a higher criterion for responding to flicker), then this might explain previous associations between CFF and subjective fatigue when watching screens,[39] even in the absence of a change in the temporal processing capability of the visual system per se. Overall, the evidence supporting CFF as a relevant measure of visual fatigue is uncertain, both in terms of theoretical support that CFF actually measures visual fatigue, as well as the magnitude of effects shown experimentally.

Whilst historically there was debate about whether the retina or cortex limited the CFF,[24] more recent psychophysical and single-cell electrophysiological studies suggest that precortical responses limit the CFF for achromatic stimuli,[29] such as those used here and in most studies investigating CFF and fatigue. Given this, there seems little reason achromatic CFF should be considered a measure of cortical function, let alone fatigue, despite this idea persisting in the literature. However, behavioural responses to purely chromatic flicker do appear to be limited by the cortex,[40] although the relationship between cortical activation by chromatic flicker and conscious perception is not trivial.[41] Therefore, it remains possible that a purely chromatic flicker task might show useful correlations with fatigue. Ensuring that the flicker task is purely chromatic is challenging, however, given that isoluminant points vary between observers.[42]

It is also worthwhile considering how influential CFF has been when assessing the efficacy of interventions. A recent systematic review investigating the efficacy of CVS interventions included CFF as one of the prespecified outcome measures of visual fatigue.[37] Of the five studies where the intervention produced a significant change in CFF (one investigating blue light-filtering lenses,[13] and four investigating complementary medicines and nutritional supplements[17,19,21,36]), there were also significant changes in other measures (e.g., subjective symptom scores). Therefore, it is unlikely that the potentially erroneous use of CFF would have altered which studies declared an intervention to be efficacious, at least within the domain of CVS. Of further note is that, of the nine studies in the review that investigated CFF,[13,17–23,36] all but one (the RCT whose data is analysed here) used a method of limits with no formal investigation of whether an observer's response criterion changed.

It may be thought that increasing the number of participants in the present study might have shifted the change from baseline correlation results from not meeting our predefined significance threshold (p = 0.05) to a statistically significant outcome ($p < 0.05$). However, irrespective of p values, the observed change from baseline Spearman correlation was −0.177, consistent with no useful correlation between CFF and overall symptom score. Hence, while the addition of data might have changed the significance level, it is unlikely to alter the overall strength of the association between parameters substantially.

Another consideration with interpreting the current findings is that only one questionnaire was investigated.[6] Nonetheless, our results are likely also applicable to other questionnaires, given the subdomains across different surveys are similar (e.g., eye strain, blurred vision, dry eye sensation and tearing), and that altering the scale of a measure (i.e., 0–5,[12] 0–10[14,30] or 0–100[43]) should not alter the magnitude or significance of a correlation. However, the validity of these questionnaires is not known. Of note is that our study population reported only mild-to-moderate visual fatigue symptoms, and so the association between CFF and severe visual fatigue symptoms is not defined from the current analysis.

In conclusion, this analysis of a double-masked RCT suggests that CFF—being among the most frequently used measure of visual fatigue, including for interventions for CVS—was not a useful surrogate for subjective symptom scores in an adult population with mild-to-moderate visual fatigue associated with computer use.

AUTHOR CONTRIBUTIONS

Sumeer Singh: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); writing – original draft (equal). **Laura E. Downie:** Conceptualization (equal); investigation (equal); methodology (equal); writing – review and editing (equal). **Andrew J. Anderson:** Conceptualization (equal); data curation (equal); methodology (equal); project administration (lead); supervision (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST

No conflicting relationships exist for any author in relation to this work.

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