

# Eliciting blinks by transcutaneous electric nerve stimulation improves tear fluid in healthy video display terminal users A self-controlled study

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#### Abstract

We aimed to elicit strong blinks among healthy video display terminal (VDT) users by periorbital transcutaneous electric nerve stimulation (TENS) and evaluate its impact on the tear fluid and visual task. Appropriate TENS conditions were evaluated to evoke strong blinks under minimum discomfort. Seventeen healthy VDT users with noninvasive Keratograph first breakup time (NIKf-BUT) 5-15 s and Ocular Surface Disease Index (OSDI) scores < 15 were recruited in this study. Before the trial, noninvasive Keratograph average breakup time (NIKa-BUT), tear meniscus height (TMH) and OSDI scores were evaluated. Before each TENS session, the volunteers played *Tetris* while the corresponding blink rate and *Tetris* scores were recorded. Then, the participants underwent 30 minutes of TENS, which evoked blinking of their right eye 20 times per minute. *Tetris* scores were evaluated again during TENS. The *Tetris* scores and corresponding blink rate were assessed after each TENS session while NIKa-BUT, TMH and OSDI scores were recorded after the third and sixth TENS sessions. We found that OSDI scores declined significantly after the sixth TENS (P = .003). The NIKa-BUT of the right eye was promoted after the sixth TENS (P = .02), and the TMH was higher after the third and sixth TENS in both eyes (P = .03, P = .03 for right eyes respectively, P = .01, P = .01 for left eyes respectively). There was no significant difference between the adjusted *Tetris* scores before and during TENS (P = .12). The blink rate before and after TENS were unaffected after 6 sessions (P = .61). The results indicated that periorbital TENS effectively ameliorated ocular irritation and improved tear secretion and tear film stability by eliciting strong blinks in healthy VDT users without disturbing the visual task.

**Abbreviations:** DES = dry eye syndromes, NIKa-BUT = noninvasive Keratograph average breakup time, NIKf-BUT = noninvasive Keratograph first breakup time, OSDI = Ocular Surface Disease Index, TENS = transcutaneous electric nerve stimulation, TMH = tear meniscus height, VDT = video display terminal.

Keywords: blinking, tear break up time, tear meniscus height, transcutaneous electric nerve stimulation, video display terminals

## 1. Introduction

Blinking is a protective reflection to remove dirt, spread tear film and promote lipid secretion.<sup>[1]</sup> This response could be affected by innocuous and noxious stimuli, including attention.<sup>[2,3]</sup> For instance, the blink rate decreases when reading or using computers,<sup>[4,5]</sup> which is closely related to the severity of computer vision syndromes and dry eye syndromes (DES).<sup>[6,7]</sup> These findings imply that blinking plays a role in the development of DES among video display terminal (VDT) users and can be a potential target to restore tear film stability.

Transcutaneous electric nerve stimulation (TENS) is a common treatment in muscle function rehabilitation and pain management.<sup>[8–12]</sup> It is capable of eliciting natural blinks, and it has been conducted mainly on patients with facial nerve disorder at present.<sup>[13–15]</sup> The parameters of periorbital TENS conducted on patients with facial nerve paralysis are probably different from those of healthy subjects. During TENS, enhanced force is evoked by stimulating terminal branches of motor axons and sensory fibers.<sup>[16,17]</sup> It indicates that unlike natural blinks, stronger contraction of periorbital muscles is developed in the blink evoked by TENS, which may promote lipid secretion of meibomian glands and thus enhance tear film stability.<sup>[18]</sup> Moreover, apart from blink elicitation, TENS is efficient in promoting local circulation,<sup>[19,20]</sup> enhancing tearing by stimulating the lacrimal gland and relieving neuropathic pain,<sup>[21–23]</sup> indicating

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that TENS itself may stimulate tear secretion and reduce ocular discomfort. Pedrotti's research confirmed such ideas, showing that periorbital TENS on DES patients improved tear film stability and relieved ocular irritation for 6 to 12 months.<sup>[24]</sup> Nonetheless, no combination of TENS and blink elicitation was practiced at present and its possible effect on tear fluid is unknown.

Several studies have focused on eliciting blinks to ameliorate DES. Notably, physical blink reminders have been investigated in different studies. For example, Miura et al<sup>[25]</sup> designed a light emitting diode timer device to remind individuals to blink, while Portello et al<sup>[7]</sup> set an audible tone ringing each 4 seconds to instruct subjects to blink. Additionally, blink reminders were also developed on electronic screens. Cardona et al<sup>[26]</sup> developed a program of transient blur and white screen on electronic devices and found it effective in enhancing blink rate when reading texts. Similarly, Nosch et al<sup>[27]</sup> induced blinking by developing blink-animation software on electronic devices and discovered that the symptoms of dry eye improved as the blink rate increased. Furthermore, Ang et al<sup>[28]</sup> reported that the wink glass that may automatically turn opaque was capable of increasing the blink frequency and maintaining the stability of tear film. Although efficient in increasing blink frequency and alleviating DES, these inventions induced blinks by similar mechanisms-developing light or sound reminders or abruptly interfering with the view to enforce users to blink, which could be annoying and induce incomplete blinks that fail to refresh tear film.<sup>[29]</sup> A new method is needed to evoke strong and complete blinking.

The occurrence of DES increases among VDT users owing to less blinking and blink elicitation is assumed to prevent DES among VDT users.<sup>[4,30]</sup> Thus, our study aimed to explore whether periorbital TENS might evoke blinking and improve tear fluid without interrupting visual tasks in healthy VDT users, which may prevent DES and could be used in daily life.

## 2. Methods

This prospective self-controlled trial was conducted at Zhongshan Ophthalmology Center. This study followed the tenets of the Declaration of Helsinki, and approval was obtained from the Ethics Committee of Zhongshan Ophthalmology Center (2018KYPJ132). Informed consent was obtained from each participant prior to the trial.

## 2.1. Exploration of appropriate TENS conditions

We recruited 18 healthy adult volunteers to explore appropriate TENS conditions for healthy individuals based on previous studies.<sup>[2,13-15,31-33]</sup> Proper TENS conditions refer to specific TENS parameters that induce complete eye closure over natural blinks under minimum discomfort. Therefore, the selection of TENS parameters was based mainly on the blink amplitude and feelings of discomfort. The positive electrode sites, current frequency and pulse width were evaluated in our study. There were 4 positive electrode sites explored in our tests based on previous studies, [2,13,14,32] including the inner canthus, outer canthus, lower eyelid and supraorbital notch. While exploring appropriate positive electrode sites, videos of tested eyes were recorded to evaluate the blink amplitude and summarize the percentage of complete blinks among all participants. The feeling of discomfort was assessed by scores ranging from 0 to 10, which were given by participants to quantify the discomfort elicited by TENS. Zero points indicated no discomfort, while 10 points revealed unbearable discomfort. The current frequency and pulse width were also explored in our study based on the feeling of discomfort. The appropriate current frequency was 100 Hz, and the proper pulse width was 200 µs (see Table S1, Supplemental Digital Content, http://links.lww.com/MD/H747 and Table S2, Supplemental Digital Content, http://links.lww.com/

MD/H748, which shows the scores of discomfort under different frequencies and pulse width). Based on the various TENS parameters and different conditions of participants' skin and muscles, the current intensity that elicits complete blinks under minimum discomfort differs from person to person; therefore, the current intensity was adjusted accordingly.

Electric stimulation was generated by the KD-2B TENS Therapy Apparatus (Yaoyangkangda Medical Equipment Limited Company, Beijing, China), and the pulse trains were biphasic and asymmetric. The pulse train lasted for 1 s per 3 s.

#### 2.2. Study population

We estimated that the enrollment of 16 participants would provide a power of 80% to detect a range of tear breakup time means from 4.6 to 7.0 after 3 measurements at an alpha significance level of 0.05 using Geisser-Greenhouse F test in the one-way repeated measure observation. Tear breakup time means were selected based on the previous research.<sup>[24]</sup> Considering a dropout rate of 20%, 20 individuals were recruited in our study. Therefore, to further analyze the impact of TENS on the tear fluid, 20 healthy VDT users were recruited from Zhongshan School of Medicine and 17 subjects (6 males and 11 females), aged 24.88 ± 2.39 years, met the inclusion criteria: noninvasive Keratograph first breakup time (NIKf-BUT) 5 to 15 seconds and Ocular Surface Disease Index (OSDI) scores < 15.<sup>[34-38]</sup> The exclusion criteria were as follows: incapable of completing the questionnaire or understanding the procedures, the presence of ocular or systemic disease or the use of topical or systemic medications that may affect the ocular surface, previous eye surgery or contact lens wear.

# 2.3. Procedure

The trial comprised 6 sessions, conducted 3 times a week, with an interval of 2 to 3 days for 2 weeks. NIKf-BUT, noninvasive Keratograph average breakup time (NIKa-BUT), tear meniscus height (TMH), OSDI scores and natural blink rate were evaluated as part of inclusion criteria and baseline evaluation (Fig. 1A). Before and after each TENS session, the blink rate while playing *Tetris* and *Tetris* scores were recorded. *Tetris* scores were measured again during TENS to assess the impact of periorbital TENS on visual tasks. Additionally, the participants were asked to rest for 30 minutes and then complete the OSDI questionnaires and undergo the measurement of NIKa-BUT and TMH after the third and sixth TENS.

### 2.4. TENS application

In each session, TENS was conducted around the right eye for 30 minutes under the appropriate conditions, which elicited periodical blinks over natural blinks monocularly with the left eye blinking freely. According to our previous observation, each pulse train elicited a corresponding blinking action on the right eye and a random blinking action on the left eye. The pulse train lasted for 1 s per 3 s, and the elicited blink rate of the right eye was 20 times per minute.

### 2.5. Assessment of NIKa-BUT, NIKf-BUT, and TMH

The assessment of NIKa-BUT, NIKf-BUT and TMH was performed using Keratograph 5M (Oculus Optikgeräte GmbH, Wetzlar, Germany). The measurement principle was described before.<sup>[39,40]</sup> Briefly, the NIKf-BUT was measured as the time between the last complete blink and the first breakup incidents. The NIKa-BUT was simultaneously obtained as the average time of all breakup incidents, which was more stable than the NIKf-BUT and thus selected as a follow-up index. Additionally, lower tear film meniscus images were captured and the TMH was measured perpendicular to the lid margin.



Figure 1. Flowchart of our study design and simplified diagram of TENS device. (A) Flowchart of TENS application and related evaluations. NIKf-BUT, NIKa-BUT, and TMH were automatically measured by Keratograph 5M. A baseline natural blink rate was observed while the participants sat relaxed, and the blink rate before and after TENS was recorded when playing *Tetris*. (B) The diagram of TENS device in our study. The device was built based on the glasses, with wires connecting the electrodes on the glasses and the TENS therapy apparatus. The symbol "–" suggested the negative electrode site, which was fixed around the temple. Symbols "①②③③" indicated the positive electrode site around the inner canthus, lower eyelid, outer canthus or supraorbital notch, respectively. NIKa-BUT = noninvasive Keratograph average break-up time, NIKf-BUT = Noninvasive Keratograph first break-up time, OSDI = Ocular Surface Disease Index, TENS = transcutaneous electric nerve stimulation, TMH = tear meniscus height.

# 2.6. Assessment of OSDI scores

OSDI scores were measured by OSDI questionnaires, ranging from 0 to 100.<sup>[37]</sup> The participants were regarded as healthy individuals when their OSDI scores were less than 15, based on previous studies.<sup>[34-38]</sup>

### 2.7. Assessment of natural blink rate

To observe the natural blink rate, study subjects were asked to sit calmly and relax while videos of their eyes were recorded by Mobile Eye Tracking Headset (Pupil Labs GmbH, Berlin, Germany) for 5 minutes, and the average blink rate was calculated. This observation was accomplished in an indoor environment with sufficient daylight, moderate temperature (25–30°C) and appropriate humidity (50%–80%).

# 2.8. Assessment of game scores and blink rate while playing Tetris

To better evaluate the effect of TENS on daily vision tasks, video game playing was selected in our study as an extreme condition of daily vision tasks. The participants were asked to play the video game *Tetris* (Duobite Information Technology Limited Company, Wuhan, China) on an iPad Air computer (Apple, San Francisco, CA) for 5 minutes before, during and after each session. Game scores and blink frequencies during playing were recorded simultaneously. If volunteers played more than 2 rounds of *Tetris* in 5 minutes, the score for each round would be added up. Additionally, the *Tetris* scores before and during TENS were modified with the score after TENS, to minimize the bias in proficiency, hand-eye coordination and individual differences.

## 2.9. Statistical analysis

The scores of discomfort, blink rate, NIKa-BUT, TMH and *Tetris* scores are presented as the mean ± standard deviation, while the OSDI scores are given as the median and interquartile range.

Categorical data are described as n (%). Statistical analysis was performed using SPSS 22.0 (IBM Inc., Chicago, IL). Student's *t* test was performed to analyze the discrepancy between the baseline blink rate and the blink rate when playing *Tetris*, while repeated-measure analysis of variance was used in the comparison among NIKa-BUT, TMH, blink rate and *Tetris* scores at different sessions. The post hoc tests, Bonferroni's test was carried out for further pairwise comparisons. The Friedman test was used to compare the OSDI scores at different times of TENS. A *P* value less than .05 was considered statistically significant.

## 3. Results

### 3.1. The appropriate TENS conditions to elicit blinks

Four positive electrode sites were explored in our trial, including the inner canthus, outer canthus, lower eyelid and supraorbital notch, as demonstrated in Figure 1B. The scores of discomfort sorted by positive electrode sites are shown in Figure 2A. The scores of discomfort at the inner canthus were lower than those at other electrode sites, suggesting that when the positive electrode was placed on the inner canthus, the majority of participants felt comfortable. The scores at the supraorbital notch were the highest due to the strong numbness around this area during TENS. In addition, complete blinks were observed in all participants when the positive electrode was placed on the inner canthus. In contrast, the percentage of complete blinks among all participants was 61.1% on the site of the outer canthus, 50.0% on the lower lid and 22.2% on the supraorbital notch (Fig. 2B). Therefore, considering the feeling of discomfort and the proportion of complete blinks, the appropriate positive electrode site was the inner canthus. For the negative electrode, it was appropriate to trigger complete blinks and cause no irritation when the negative electrode was placed around the temple based on our pilot experiment.

Based on our experiment (see Table S1, Supplemental Digital Content, http://links.lww.com/MD/H747 and Table S2, Supplemental Digital Content, http://links.lww.com/MD/H748, which shows scores of discomfort under different frequencies



Figure 2. The scores of discomfort and percentage of complete blink in the exploration of positive electrode sites. (A) The average discomfort scores at different positive electrode sites. The scores of discomfort ranged from 0 to 10, which was given by participants to quantify the discomfort elicited by TENS. Data are shown as the mean ± standard deviation. (B) Percentage of complete blink elicited among all study subjects at different positive electrode sites. Percentage of complete blink = the sum of participants whose blink was complete under TENS elicitation/total amount of participants. TENS = transcutaneous electric nerve stimulation.

and pulse width) and previous researches,  $^{[2,13-15,31-33]}$  the appropriate TENS conditions included positive electrode placed near the inner canthus, negative electrode fixed near the temple of the same side, current frequency 100 Hz, pulse width 200 µs and current intensity 4 to 7 mA, which was adjusted individually to induce complete blinks and the least discomfort. In addition, the stimulation interval was set as electrical stimulation for 1 s per 3 s.

#### 3.2. The effect of TENS on the blink frequency

During periorbital TENS, the blink rate of participants' right eye was increased to 20 times per minute. We evaluated the blink rate before and after TENS to determine whether TENS affects the natural blink rate. As presented in Figure 3, the baseline blink rate of enrolled individuals was 13.42±7.49 times per minute when the participants were sitting relaxed. The blink rate of the right eye was 20 times per minute during TENS, determined by pulse trains. The blink rate of the left eve varied among individuals as no intervention was conducted around the left eye and the left eye blinked on a random basis during each pulse train. The baseline blink rate was significantly higher than the blink rate while playing Tetris (P = .001). There was no obvious difference between the blink rate before and after TENS (P = .20). Additionally, the blink frequency remained stable after 6 sessions (P = .61), suggesting that participants' natural blink frequencies were unaffected after 6 sessions of TENS.

# 3.3. The effect of TENS on the OSDI score

OSDI scores were assessed before the first TENS and after the third and sixth TENS to observe the changes in ocular complaint. As presented in Figure 4, the OSDI score of all subjects was 2.10 (0.00–10.40) before the trial. Moreover, the OSDI score was 2.10 (0.00–5.60) after the third TENS and further decreased to 0.00 (0.00–2.10) after the sixth TENS. There was a statistically significant difference between the OSDI scores before TENS and after the sixth TENS (P = .003).

## 3.4. The effect of TENS on the NIKa-BUT and TMH

To record the changes in tear film stability and tear secretion, the NIKa-BUT and TMH of both eyes were evaluated before the trial and after the third and sixth TENS sessions. As TENS elicited strong blinks in participants' right eye, NIKa-BUT of the right eye was apparently promoted, as displayed in Figure 5A. The average NIKa-BUT of the right eye was  $13.25 \pm 4.26$  s at baseline and  $16.00 \pm 5.68$  seconds after the third TENS, but the difference was not statistically significant (P = .30). After the sixth TENS, the NIKa-BUT of the right eye increased to  $17.46 \pm 3.74$  seconds, which was notably higher than the NIKa-BUT before TENS (P = .02). In contrast with the right eye, the NIKa-BUT of the left eye did not manifest an obvious change after the third or the sixth TENS (P = .16).

There were remarkable changes in the TMH of both eyes (Fig. 5B). TMH of the right eye was  $0.22 \pm 0.09$  mm at baseline and increased to  $0.28 \pm 0.12$  mm after 3 TENS sessions (*P* = .03). The TMH of the right eye was  $0.27 \pm 0.10$  mm after the sixth TENS session, which was also significantly higher than the TMH before TENS (*P* = .03). The TMH of the left eye showed a tendency similar to that of the right eye. The TMH of the left eye before TENS was lower than the TMH after the third TENS (0.19 ± 0.06 mm vs 0.27 ± 0.12 mm, respectively, *P* = .01) and the TMH after the sixth TENS (0.19 ± 0.06 mm vs 0.26 ± 0.12 mm, respectively, *P* = .01).

#### 3.5. The effect of TENS on the Tetris scores

Study subjects were arranged to play *Tetris* before, during and after TENS to evaluate whether periorbital TENS influenced daily visual tasks. To reduce the bias caused by proficiency, individual difference and hand-eye coordination, the *Tetris* scores before and during TENS were modified with the score after TENS. The *Tetris* scores are displayed in Figure 6. Due to proficiency in *Tetris*, the average scores after TENS were higher than those before and during TENS. Hence, the adjusted scores before and during TENS, which were subtracted from the score after TENS, were negative. The adjusted scores fluctuated without obvious tendency. In addition, the modified scores during TENS were similar to those before TENS (P = .12).



**Figure 3.** Blink frequency of study subjects when relaxing or playing *Tetris* before and after TENS. A baseline blink rate (0 TENS session) was observed by recording the eye movement of study subjects for 5 min when they were sitting quietly and relaxing. In addition, the blink frequencies were also recorded while the volunteers were playing *Tetris* before and after TENS. Blink frequency was calculated as the average rate in 5 mins. Student's t test was performed to compare the baseline blink rate with the blink rate during *Tetris* playing and repeated-measure analysis of variance were performed to analyze the discrepancy among the blink rate at different sessions of TENS. Data are presented as the mean and standard deviation. \*\*When compared with the blink rate sitting relaxed, the difference was statistically significant, *P* < .01. TENS = transcutaneous electric nerve stimulation.



**Figure 4.** OSDI scores before TENS and after the third and sixth TENS. The OSDI score ranged from 0 to 100. Data are presented as the median and quartile. The Friedman test was conducted to compare OSDI scores at different TENS sessions. \*\* P < .01. OSDI = Ocular Surface Disease Index, TENS = transcutaneous electric nerve stimulation.

# 4. Discussion

Blinking is a natural mechanism to refresh tear film.<sup>[1]</sup> Previous studies showed that the blink rate dropped when using VDTs and inducing blinks was capable of restoring tear film stability and ameliorating dry eye symptoms.<sup>[2,5,27,28]</sup> Electrical stimulation was able to evoke a strong blink,<sup>[13–17]</sup> yet the parameters and the impact of TENS on the tear fluid were unknown. In this



🖾 Before TENS 🎞 After 3rd TENS 🔤 After 6th TENS

Figure 5. The impact of TENS on the NIKa-BUT and TMH of both eyes. The NIKa-BUT and TMH were automatically detected by Keratograph 5M. Statistical differences were analyzed with repeated-measure analysis of variance and Bonferroni's test. (A) The influence of TENS on the NIKa-BUT of both eyes. (B) The influence of TENS on the TMH of both eyes. Data are displayed as the mean  $\pm$  standard deviation. \*P < .05. NIKa-BUT = noninvasive Keratograph average break-up time, TENS = transcutaneous electric nerve stimulation, TMH = tear meniscus height.



Figure 6. The *Tetris* scores before and during TENS at different TENS sessions. Participants were asked to play *Tetris* on an iPad Air computer before, during and after TENS for 5 min to evaluate the influence of TENS on the visual task. The scores were added if the volunteers played  $\geq 2$  rounds. Additionally, in order to minimize the bias in proficiency, hand-eye coordination and individual difference, scores before and during TENS were adjusted by subtracting the scores after TENS. The scores after TENS were higher than the scores before and during TENS due to proficiency, thus the adjusted scores before and during TENS were negative. TENS = transcutaneous electric nerve stimulation.

study, periorbital TENS was conducted on healthy VDT users under appropriate conditions to elicit strong blinks, and notable changes were observed in tear film stability, tear secretion and ocular irritation without influencing the daily visual task of the participants.

Electrical stimulation has previously been applied to induce blinks in facial paralysis patients, and the related parameters have been explored before.<sup>[13-15]</sup> However, the parameters explored before were possibly different from the parameters applied to healthy individuals. Therefore, TENS conditions were evaluated again in our study. The selection of positive electrode sites was based on previous studies.<sup>[2,13,14,32]</sup> Additionally, based on our pre-experiment, the various sites of the negative electrode had similar effects on blinking; thus, the negative electrode was placed around the temple. For the current frequency, the frequency 50 to 200 Hz was previously used.<sup>[13,15,32]</sup> Based on our results, the current frequency was set at 100 Hz in our study. The range of the appropriate pulse width was introduced as 100 to 200 µs in most studies and 400 to 1000 µs in a few studies.<sup>[2,13-15,31-33]</sup> In our study, the pulse width was 200 µs based on the discomfort feeling. Moreover, the stimulus duration was adjusted to 1 s per 3 s in our study, as shorter stimulus durations were more likely to induce partial blinks and transient eye-closing periods in our pre-experiment, which was insufficient to renew the tear film.<sup>[29]</sup>

Under appropriate TENS conditions, periorbital TENS on a regular basis is beneficial for healthy individuals with relatively shorter NIKf-BUT by eliciting blinks. Our study subjects were healthy youths in the medical school who used VDTs frequently and were at risk of DES. Individuals with NIKf-BUT > 15 seconds were excluded, as their NIKf-BUT was much longer than the diagnostic criterion of DES (tear break up time < 10 seconds), indicating a low risk of DES.<sup>[41,42]</sup> In addition, individuals whose NIKf-BUT < 5 seconds were also excluded to avoid asymptomatic dry eye patients.<sup>[43]</sup> Although participants were healthy VDT users without obvious ocular symptoms, their NIKa-BUTs and TMH increased and their OSDI scores decreased after 6 TENS sessions, conveying that periorbital TENS was effective in preventing DES among VDT users.

Periorbital TENS improved tear film stability mainly by increasing the blink rate and eliciting strong blinks. The baseline blink rate was  $13.42 \pm 7.49$  times per minute. As the pulse train, which may stimulate monocular blinks stronger than natural blinks, occurred every 3 seconds, the blink rate of our participants increased to 20 times per minute during TENS. Increased blink rate is beneficial to tear film stability and tear meniscus recovery.<sup>[27,28,44]</sup> The blink rate before and after TENS were unaffected after 6 sessions, indicating that the blink rate was increased only during TENS and the nature of the orbicularis oculi muscle was unaffected without TENS. Additionally, as TENS can stimulate both terminal branches of motor axons and sensory fibers,<sup>[16,17]</sup> TENS-elicited blinks are stronger than natural blinks, which is consistent with the feedback of enrolled subjects. Stronger contraction of the orbicularis oculi muscle enhances the lipid secretion of meibomian glands and tear refreshment,<sup>[18,45,46]</sup> and may subsequently promote tear film stability and tear secretion.

Changes in tear film stability, tear secretion and ocular irritation may also result from the inherent properties of TENS. TENS is efficient in promoting local circulation,<sup>[19,20]</sup> enhancing tearing by stimulating the lacrimal gland and relieving neuropathic pain,<sup>[21,22,47-49]</sup> which is a common syndrome in dry eye.<sup>[50,51]</sup> This is supported by previous studies. Pedrotti et al<sup>[24]</sup> demonstrated that TENS around the temporal area and lower eyelid in DES patients improved tear film stability and relieved ocular irritation for 6 to 12 months. Similarly, Tseng et al<sup>[52]</sup> discovered that traditional electro-acupuncture therapy around the eyes was effective in stimulating tear secretion in DES patients. It indicates that periorbital TENS enhances tear film stability, promotes tear secretion and relieves ocular irritation by both blink elicitation and its unique property. In general, periorbital TENS increases tear film stability and tear secretion, which is beneficial for VDT users in preventing DES and relieving ocular discomfort.

The changes in the NIKa-BUT and TMH were slightly different between the left and right eyes. There were remarkable changes in the NIKa-BUT of the right eye, the eye accepted TENS, instead of the left eye. A possible explanation is that the blink amplitude triggered by TENS was stronger than the natural blink.<sup>[16,17]</sup> Therefore, more lipids were squeezed out and released into the tear film after TENS, which enhanced the tear film stability.<sup>[46]</sup> Nevertheless, the change in TMH after TENS was similar in both eyes, conveying that the influence of TENS on tear secretion may be binocular, even though TENS was conducted only around the right eye. The neurosecretory mechanism might be involved in the change of TMH.<sup>[22]</sup> Further studies are needed to determine the underlying mechanism of this phenomenon.

#### 5. Conclusion

TENS is a mature and effective technique to evoke blinking. The periorbital TENS, which may elicit a strong blink in healthy VDT users, was capable of promoting tear film stability, enhancing tear secretion and alleviating ocular surface discomfort without affecting daily visual tasks and inherent blinks. More work should be done to evaluate the long-term effects of periorbital TENS and its further application in DES patients.

#### Author contributions

Conceptualization: Kaili Wu. Funding acquisition: Kaili Wu. Investigation: Weiting Zeng, Han Lou, Kunke Li. Methodology: Weiting Zeng, Han Lou, Kunke Li. Resources: Quanbin Huang, Xiuping Liu, Kaili Wu. Supervision: Kaili Wu. Writing – original draft: Weiting Zeng. Writing – review & editing: Kaili Wu.

#### References

- Rodriguez JD, Lane KJ, Ousler GW, 3rd, et al. Blink: characteristics, controls, and relation to dry eyes. Curr Eye Res. 2018;43:52–66.
- [2] Evinger C, Bao JB, Powers AS, et al. Dry eye, blinking, and blepharospasm. Mov Disord. 2002;17(Suppl 2):S75–8.
- [3] Schicatano EJ. The effects of attention on the trigeminal blink reflex. Percept Mot Skills. 2016;122:444–51.
- [4] Argiles M, Cardona G, Perez-Cabre E, et al. Blink rate and incomplete blinks in six different controlled hard-copy and electronic reading conditions. Invest Ophthalmol Vis Sci. 2015;56:6679–85.
- [5] Cardona G, Garcia C, Seres C, et al. Blink rate, blink amplitude, and tear film integrity during dynamic visual display terminal tasks. Curr Eye Res. 2011;36:190–7.
- [6] Patel V, Daya SM, Lake D, et al. Blink lagophthalmos and dry eye keratopathy in patients with non-facial palsy: clinical features and management with upper eyelid loading. Ophthalmology. 2011;118:197–202.
- [7] Portello JK, Rosenfield M, Chu CA. Blink rate, incomplete blinks and computer vision syndrome. Optometry Vision Sci. 2013;90:482–7.
- [8] Johnson MI. Transcutaneous electrical nerve stimulation (TENS) as an adjunct for pain management in perioperative settings: a critical review. Expert Rev Neurother. 2017;17:1013–27.
- [9] Proctor ML, Smith CA, Farquhar CM, et al. Transcutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhoea. Cochrane Database Syst Rev. 2002;1:Cd002123.
- [10] Straube A, Ellrich J, Eren O, et al. Treatment of chronic migraine with transcutaneous stimulation of the auricular branch of the vagal nerve (auricular t-VNS): a randomized, monocentric clinical trial. J Headache Pain. 2015;16:543.
- [11] Eraslan L, Yuce D, Erbilici A, et al. Does Kinesiotaping improve pain and functionality in patients with newly diagnosed lateral epicondylitis? Knee Surg Sports Traumatol Arthrosc. 2018;26:938–45.

- [12] Jones S, Man WD, Gao W, et al. Neuromuscular electrical stimulation for muscle weakness in adults with advanced disease. Cochrane Database Syst Rev. 2016;10:Cd009419.
- [13] Frigerio A, Heaton JT, Cavallari P, et al. Electrical stimulation of eye blink in individuals with acute facial palsy: progress toward a bionic blink. Plast Reconstr Surg. 2015;136:515e–23e.
- [14] Gittins J, Martin K, Sheldrick J, et al. Electrical stimulation as a therapeutic option to improve eyelid function in chronic facial nerve disorders. Invest Ophthalmol Vis Sci. 1999;40:547–54.
- [15] Jie T, Zhiqiang G, Guodong F, et al. The effective stimulating pulse for restoration of blink function in unilateral facial nerve paralysis rabbits, verified by a simple FES system. Eur Arch Otorhinolaryngol. 2016;273:2959–64.
- [16] Lake DA. Neuromuscular electrical stimulation. An overview and its application in the treatment of sports injuries. Sports Medicine (Auckland, NZ). 1992;13:320–36.
- [17] Requena Sanchez B, Padial Puche P, Gonzalez-Badillo JJ. Percutaneous electrical stimulation in strength training: an update. J Strength Cond Res. 2005;19:438–48.
- [18] Olzynska A, Cwiklik L. Behavior of sphingomyelin and ceramide in a tear film lipid layer model. Ann Anatomy Anatomischer Anzeiger. 2017;210:128–34.
- [19] Cramp FL, McCullough GR, Lowe AS, et al. Transcutaneous electric nerve stimulation: the effect of intensity on local and distal cutaneous blood flow and skin temperature in healthy subjects. Arch Phys Med Rehabil. 2002;83:5–9.
- [20] Vieira PJ, Ribeiro JP, Cipriano G, Jr, et al. Effect of transcutaneous electrical nerve stimulation on muscle metaboreflex in healthy young and older subjects. Eur J Appl Physiol. 2012;112:1327–34.
- [21] Brinton M, Chung JL, Kossler A, et al. Electronic enhancement of tear secretion. J Neural Eng. 2016;13:016006.
- [22] Brinton M, Kossler AL, Patel ZM, et al. Enhanced tearing by electrical stimulation of the anterior ethmoid nerve. Invest Ophthalmol Vis Sci. 2017;58:2341–8.
- [23] Zayan K, Aggarwal S, Felix E, et al. Transcutaneous electrical nerve stimulation for the long-term treatment of ocular pain. Neuromodulation. 2020;23:871–7.
- [24] Pedrotti E, Bosello F, Fasolo A, et al. Transcutaneous periorbital electrical stimulation in the treatment of dry eye. Br J Ophthalmol. 2017;101:814–9.
- [25] Miura DL, Hazarbassanov RM, Yamasato CK, et al. Effect of a light-emitting timer device on the blink rate of non-dry eye individuals and dry eye patients. Br J Ophthalmol. 2013;97:965–7.
- [26] Cardona G, Gomez M, Quevedo L, et al. Effects of transient blur and VDT screen luminance changes on eyeblink rate. Cont Lens Anterior Eye. 2014;37:363–7.
- [27] Nosch DS, Foppa C, Toth M, et al. Blink animation software to improve blinking and dry eye symptoms. Optometry Vision Sci. 2015;92:e310–5.
- [28] Ang CK, Mohidin N, Chung KM. Effects of wink glass on blink rate, nibut and ocular surface symptoms during visual display unit use. Curr Eye Res. 2014;39:879–84.
- [29] Su Y, Liang Q, Su G, et al. Spontaneous eye blink patterns in dry eye: clinical correlations. Invest Ophthalmol Vis Sci. 2018;59:5149–56.
- [30] Uchino M, Yokoi N, Uchino Y, et al. Prevalence of dry eye disease and its risk factors in visual display terminal users: the Osaka study. Am J Ophthalmol. 2013;156:759–66.
- [31] Conte A, Fabbrini G, Belvisi D, et al. Electrical activation of the orbicularis oculi muscle does not increase the effectiveness of botulinum toxin type A in patients with blepharospasm. Eur J Neurol. 2010;17:449–55.

- [32] Frigerio A, Cavallari P. A closed-loop stimulation system supplemented with motoneurone dynamic sensitivity replicates natural eye blinks. Otolaryngol Head Neck Surgery. 2012;146:230–3.
- [33] Miwa H, Nohara C, Hotta M, et al. Somatosensory-evoked blink response: investigation of the physiological mechanisms. Brain. 1998;121(Pt 2):281–91.
- [34] Garcia-Resua C, Pena-Verdeal H, Giraldez MJ, et al. Clinical relationship of meibometry with ocular symptoms and tear film stability. Cont Lens Anterior Eye. 2017;40:408–16.
- [35] Gonzalez-Cavada J, Martin R, Pinero DP. Clinical characterization of asymptomatic or minimally symptomatic young patients showing signs compatible with dry eye: a pilot study. Eye Contact Lens. 2015;41:171-6.
- [36] Ring MH, Rabensteiner DF, Horwath-Winter J, et al. Introducing a new parameter for the assessment of the tear film lipid layer. Invest Ophthalmol Vis Sci. 2012;53:6638–44.
- [37] Schiffman RM, Christianson MD, Jacobsen G, et al. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000;118:615–21.
- [38] Seres C, Quevedo L, Cardona G, et al. Tear break-up time for tear film evaluation: Are moistening solutions interchangeable? Cont Lens Anterior Eye. 2015;38:272–6.
- [39] Jiang Y, Ye H, Xu J, et al. Noninvasive Keratograph assessment of tear film break-up time and location in patients with age-related cataracts and dry eye syndrome. J Int Med Res. 2014;42:494–502.
- [40] Tian L, Qu JH, Zhang XY, et al. Repeatability and reproducibility of noninvasive keratograph 5M measurements in patients with dry eye disease. J Ophthalmol. 2016;2016:8013621.
- [41] Thulasi P, Djalilian AR. Update in current diagnostics and therapeutics of dry eye disease. Ophthalmology. 2017;124(11s):S27–33.
- [42] Hashemi H, Khabazkhoob M, Kheirkhah A, et al. Prevalence of dry eye syndrome in an adult population. Clin Exp Ophthalmol. 2014;42:242–8.
- [43] Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. Deutsches Arzteblatt international. 2015;112:71–81; quiz 82.
- [44] Huang Y, Sheha H, Tseng SC. Conjunctivochalasis interferes with tear flow from fornix to tear meniscus. Ophthalmology. 2013;120:1681–7.
- [45] Garaszczuk IK, Mousavi M, Cervino Exposito A, et al. Evaluating tear clearance rate with optical coherence tomography. Cont Lens Anterior Eye. 2018;41:54–9.
- [46] Wan T, Jin X, Lin L, et al. Incomplete blinking may attribute to the development of meibomian gland dysfunction. Curr Eye Res. 2016;41:179–85.
- [47] Colloca L, Ludman T, Bouhassira D, et al. Neuropathic pain. Nat Rev Dis Primers. 2017;3:17002.
- [48] Kilinc M, Livanelioglu A, Yildirim SA, et al. Effects of transcutaneous electrical nerve stimulation in patients with peripheral and central neuropathic pain. J Rehabil Med. 2014;46:454–60.
- [49] Zhang R, Lao L, Ren K, et al. Mechanisms of acupuncture-electroacupuncture on persistent pain. Anesthesiology. 2014;120:482–503.
- [50] Galor A, Levitt RC, Felix ER, et al. Neuropathic ocular pain: an important yet underevaluated feature of dry eye. Eye. 2015;29:301–12.
- [51] Galor A, Moein HR, Lee C, et al. Neuropathic pain and dry eye. Ocul Surf. 2018;16:31–44.
- [52] Tseng KL, Liu HJ, Tso KY, et al. A clinical study of acupuncture and SSP (silver spike point) electro-therapy for dry eye syndrome. Am J Chin Med. 2006;34:197–206.