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Frequent spontaneous eyeblink activity associated with reduced conjunctival surface (trigeminal nerve) tactile sensitivity

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Abstract

Background A number of recent studies have reported high spontaneous eyeblink rate (SEBR) values in apparently normal subjects, but the reasons for this are unclear.

Methods An assessment was made of SEBR, in 60 educated adult male subjects aged between 22 and 40 years, over a period of 5 min in silence. Half of the subjects were classified as having frequent eyeblink activity. All subjects also had their corneal and conjunctival touch (tactile) sensitivity assessed with a Cochet-Bonnet aesthesiometer immediately after the video recording of SEBR.

Results SEBR ranged from 4.6 to 43.5 (mean 18.6) eyeblinks/min. The SEBR was 26.8 ± 6.0 eyeblinks/min for those with frequent eyeblink activity as compared to just 10.3 ± 3.5 eyeblinks/min for those with normal eyeblink activity (p<0.001). There was no difference in palpebral aperture or exposed ocular surface area between the two groups. The average central corneal sensitivity was only marginally different between the two groups ($56.8 \pm 2.8 \text{ mm vs } 58.5 \pm 2.3 \text{ mm}$) but the conjunctival threshold sensitivity was substantially different (at $23.8 \pm 4.3 \text{ mm vs } 28.5 \pm 3.5 \text{ mm}$; p<0.001). SEBR was inversely correlated with the conjunctival sensitivity in those with frequent eyeblink activity (p<0.001).

Conclusions Our study provides a clue as to the mechanism of inhibition of spontaneous eyeblink activity, namely that a certain level of ocular surface (conjunctival) sensitivity is required to keep SEBR low.

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Department of Vision Sciences, Glasgow-Caledonian University, Cowcaddens Road, Glasgow G4 OBA, Scotland e-mail: m.doughty@gcal.ac.uk **Keywords** Eyeblinking · Primary gaze · Corneal tactile sensitivity · Conjunctival tactile sensitivity

Introduction

A spontaneous eyeblink activity is characteristic of normal healthy and awake individuals [1-7]. It can be easily assessed by counting or recording (including by electromyography) the number of eyelid closure events over a finite period of time to allow calculation of a spontaneous eyeblink rate (SEBR; also known as the eyeblink rate or EBR, or simply as the blink rate or BR).

Observations on healthy subjects reveal a wide range of SEBR values from as low as around 2 eyeblinks/min to as high as 55 eyeblinks/min [7-11], regardless of whether manual or more automated methods of eyeblink recording are used. The SEBR can change substantially according to the status of a subject while the eyeblink observations are being made. From a simple and task-related perspective, it can also be shown that the SEBR values broadly segregate into three groups [7]. Lowest values of SEBR can be expected to be associated with reading-related activities, while commonly-reported 'normal' values are those associated with a resting state, without speaking and in silence (also considered as being 'unoccupied' activity). In the absence of any disease or neurological problems, the highest SEBR values can be expected to be associated with subjects engaged in some form of conversation, or other substantial person-to-person interaction [7], perhaps even in television newscasters [10].

There are other reasons why SEBR can increase. The exposure of the eyes and facial skin to any form of adverse environment can be expected to be associated with an increased SEBR, which is presumably linked to stimulation of exogeneous (trigeminal) receptors. Such adverse stimuli include exposure to pollutants, noxious chemicals, extremes of temperature and/or humidity, and other physical factors such as air flow (drafts) across the eyes and face [12-16]. Eyelid closure can also be induced by more obvious tactile stimulation, with a blink reflex being elicited by mechanical contact of the cornea [17-19].

A number of investigators have undertaken studies to assess whether the spontaneous eyeblink rate can be linked to actual measurements of ocular surface sensitivity. A substantial reduction in corneal sensitivity, achieved with topical anaesthetic evedrops, has been repeatedly observed to be associated with a similarly marked reduction in SEBR [20-24]. This overall effect does not mean however that it will be observed in all subjects [20-22, 24], and no substantial effects of presenting a presumed topical anaesthetic (cocaine as eyedrops) were noted on eyeblink activity in a much older study [1]. An analysis has been made to see if the reduction in SEBR could be systematically correlated to the reduction in corneal sensitivity by anaesthetic action and, while a trend was evident $(r \ge 0.41)$, it was not statistically significant (p>0.1) [21]. In a later analysis, with a much larger number of subjects, the conclusion was drawn that there was no obvious correlation between preanaesthetic and post-anaesthetic eyeblink rates [24]. From these studies [20–24], it might be concluded that, despite the overall effect, a certain level of corneal sensitivity could not be linked to a specific eyeblink rate, at least over the relatively narrow range of normal eyeblink activities [7].

Our study was designed to further explore whether SEBR could be linked to objective measures of ocular surface sensitivity, both by specifically comparing larger and better matched groups of individuals with normal and frequent eyeblink activity, and also extending the analyses to include evaluation of the bulbar conjunctiva.

Materials and methods

Sixty healthy male adults voluntarily agreed to serve as subjects, and were paid a small honorarium for their participation. After approval of all protocols by Glasgow-Caledonian University ethics committee, subjects were recruited by personal contact or by an e-mail-based request for participants. The subjects, all academic staff members or graduate students, were given a verbal and written explanation of the protocols, and then provided written consent. The criteria for inclusion were that the subjects should be aged between 20 and 40 years, be male, ambulatory and without any major health problems. Subjects should not be taking medications for cardiovascular or endocrine conditions, or any form of neurological or neuromuscular disorders. The subjects should be free of any significant eye disease, have a negative history for ocular surgery, habitual contact lens wear or any clinically significant binocular vision problems. Lastly, the subjects should not have significant refractive error (>2.5 DS) that could interfere with the simple viewing task presented during eyeblink recording.

On arrival at the eye clinic examination room between 11.00 and 17.00 hours to limit the chance of any diurnal effects on eyeblink rate [25], all subjects were asked to be seated and then complete a questionnaire on eye symptoms, about health and medication use [26]. Details of any ocular symptoms were obtained, along with information on any conditions where eye discomfort was noted (provocative stimuli). To compare such responses, the number of reported symptoms was added up, a note taken of how frequently any symptoms might be experienced, and also whether there were any known stimuli that provoked their symptoms (even if these were not being experienced at the time of assessment). A cumulative weighted score was calculated, the highest values of which could be over 20 for an individual with severe dry eye problems. The questionnaire also collected data about smoking and alcohol use. This questionnaire was completed over a 5 min period as the subjects adapted to the lighting, temperature and ambient humidity of the room. The lighting level at the target was set at close to 350 lux by the cool white fluorescent room lighting, and the average values for temperature and humidity were routinely between 18°C and 21°C and 31% and 40% respectively, as provided by local and central room environment controls. Once the questionnaire was completed and the investigators were satisfied that the subject was suitable for further evaluation, assessments were made of both the eyeblink activity and of the sensitivity of the ocular surface to a tactile (touch) stimulus.

The spontaneous eyeblink activity in primary eye gaze was recorded in a very specific fashion following an established protocol [24, 27, 28]. No specific training sessions were undertaken, and a video recording was made over a 5-min period with the subject and examiner maintaining silence, and with no cues given as to the passage of time. A digital camera system was used at 25 f.p.s. so that the occurrence of any eyeblink event could be verified by frame replay [24], as opposed to using a paper trace-based event marker [27]. An eyeblink event was considered as any substantial downward movement of the upper eyelid regardless of whether the movement was a complete one (resulting in complete eyelid closure), although any eyelid twitching was ignored. After the eyeblink recording, the ocular surface sensitivity of the right eye was assessed with a Cochet-Bonnet aesthesiometer [29]. The instrument was mounted on a customdesigned cradle attached to a slit-lamp biomicroscope [24]

such that the location, angle and speed of presentation of the nylon filament could be smoothly controlled. For these studies, the tactile sensitivity was assessed close to the apex of the cornea (essentially the pupil centre as judged visually) and on the nasal bulbar conjunctiva at a position 3 to 4 mm from the limbus along the horizontal meridian as judged by simple visual inspection. The subject would be asked to redirect their gaze (i.e. outwards for the nasal measurements) prior to starting the stimulus cycle. Assessment of the tactile threshold was made by defining that length of the filament which was just detectable by the subject in two of three randomly repeated trials, with stimuli either side of the threshold being interspersed with repeated measures once the threshold range was identified. Dummy presentations were routinely used to check the tactile threshold, especially if there was some uncertainty, and care was taken not to repeat the contacts at such a close interval that habituation might have developed. The subjects were advised that they could blink if needed any point during the assessment, and even reposition themselves if this made them feel more comfortable. Biomicroscopy, with and without fluorescein staining (Fluorets® strip, wetted with preservative-free saline), was then undertaken. For bulbar redness and fluorescein staining, the 5-point CCLRU scheme was used [30]. Eyelid eversion was also undertaken, after fluorescein staining, to check for any substantial tarsal plate abnormalities or inflammation. From external eye images, the exposed ocular surface area was measured [9].

All data were entered into spread sheets in Systat (Systat, Evanston, IL, USA) for reporting of general statistics (mean, median, SD) and data sets were checked for normality using the default option of the Shapiro-Wilk statistic as incorporated into Systat. The distribution of data was also assessed by calculation of the coefficient of skewness. Assessment of the variability of the minute-byminute values for SEBR was calculated from the standard deviation (SD) and then a normalised SD (the coefficient of variation, COV) also calculated. Comparisons between data sets was done by ANOVA (Mann-Whitney rank test) and a linear regression analysis was used to compare ocular surface sensitivity data to the eyeblink activity, with the goodness of fit being assessed by the Pearson (r) or Spearman (r_s) correlation coefficients. For comparisons and regressions, the level of significance was set at p < 0.05.

Results

A total of 60 male subjects were evaluated, with ages ranging from 22 to 40 years (average 31.6 ± 4.7 years). Overall, these subjects reported no substantial eye discomfort or problems, but half of them did report some mild ocular complaints such as slight dry eve symptoms or slight eye itching symptoms. Overall, the 60 subjects reported a weighted average number of symptoms of 1.48, but with no subject reporting more than 2 symptoms, and with only four of them reporting experiencing any symptoms on a frequent basis (as opposed to only sometimes). Overall, the external eye appearances were considered to be generally unremarkable, although nearly half of them had very slight hyperaemia (grade 0.5) and mild Meibomian gland inflammation that was consistent with the mild symptoms reported. No significant fluorescein staining was observed (no grade higher than 1), nor were there any signs of aesthesiometer filament damage to the corneal or conjunctival surfaces. External eye photographs indicated normal palpebral aperture features, with the exposed ocular surface area (EOSA) values in primary gaze ranging from 1.055 to 2,782 cm², with an overall mean of 1.553 ± 0.336 cm².

Only five subjects reported the use of any medications; these were all non-prescription (OTC) and not of a type considered as exemptions (see earlier). No subject indicated notable alcohol use, with any indicated consumption being below 14 units/week. Just 11 subjects indicated a current smoking history, and in all cases the use was light.

For the 60 subjects, the SEBR values, averaged over a 5-min period, ranged from 4.6 to 43.5 eyeblinks/min, with a median value of 19.2. Over the 5-min period, the eyeblinking did fluctuate somewhat (Fig. 1). The intra-subject variability, based on the SD of the eyeblink rate over the 5 min, was 3.7 eyeblinks/min. As can be seen in Fig. 1, there appeared to be a slight time-related change, in that the median values were lower in the first minute (at 17.2) than in the last minute of recording (at 19.1). However, neither a repeated ANOVA (p>0.273) nor a linear regression analysis (p=0.197) indicated any statistically significant change of SEBR over time.

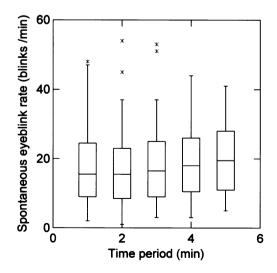


Fig. 1 Box plot to show time-related stability of spontaneous eyeblink rate for all 60 subjects

An analysis to assess whether there was any predictable relationship between the exposed ocular surface area in primary eye gaze and the SEBR averaged over the 5 minutes revealed no interdependency (Fig. 2). A linear regression analysis confirmed a lack of statistical correlation between the two variables (p=0.854, r=0.024).

Half of the subjects were considered to show frequent (as opposed to normal) spontaneous eyeblink activity. The age of the subjects in either group, selected for SEBR, was the same, with averages of 30.8 and 32.5 years respectively. Of those subjects reporting any ocular symptoms, 11 (of 30) were those in the frequent eyeblink group and 19 in the normal eyeblink group. The averaged symptom score in those with frequent eyeblink activity was slightly lower (at 1.33) than those in the normal group (at 1.63), but neither group of subjects were considered as having substantial ocular symptoms. There were no obvious differences in external eye characteristics (e.g. in any bulbar hyperaemia) or differences in the palpebral aperture height or the calculated exposed ocular surface area when comparing the two groups (Kruskal–Wallis ANOVA, $p \ge 0.438$).

The normal group of subjects had averaged SEBR values (over the 5-minute period) from just 4.6 to 18.8 eyeblinks/ min and an overall mean value of 10.3 ± 3.5 eyeblinks/min. The intra-subject variability in SEBR was 2.7 eyeblinks/min. Those subjects with frequent eyeblink activity had SEBR values ranging from 19.6 to 43.5 eyeblinks/min. Their mean SEBR was 26.8±6.0 eyeblinks/min, and this was very different from those with normal eyeblink rates (p<0.001). There was no obvious difference in the intra-subject variability in SEBR between the groups, for although the absolute value was slightly higher in those with frequent eyeblink activity (SD=4.7 eyeblinks/min), the mean SEBR

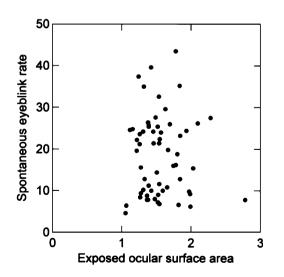


Fig. 2 Scatterplot to show the lack of any relationship between the spontaneous eyeblink rate (in eyeblinks/min) and the exposed ocular surface area (in cm^2)

was higher as well. Statistical comparisons, based on the COV, indicated no difference in the intra-subject variability in SEBR between the two groups (p=0.699). While specific measurements of eye position in relation to the target line of sight were not made, scrutiny of the video records did not show that those subjects with frequent eyeblink activity, for example, showed notable saccadic eye movements during the course of the recordings; i.e., the higher eyeblink rate was not associated with the occurrence of involuntary saccades. There was, as with the normal subjects, a slight time-related trend, in that the median SEBR values shifted from 24.9 in the first minute to 28.0 in the final minute, but this change could not be shown to be statistically significant ($p \ge 0.433$).

For the 60 subjects, the mean central corneal tactile sensitivity threshold was 57.7 ± 2.7 mm. As shown in Fig. 3, all but one subject could detect either the 60 mm or 55 mm nylon filament presented to the central corneal region. Figure 3 also shows that there was no obvious relationship between the corneal threshold and SEBR. The mean corneal sensitivity values were also not substantially different when comparing those with normal eyeblink activity (i.e. SEBR values of \leq 19 eyeblinks/min) with those having frequent eyeblink activity, although the mean values were marginally lower in those with frequent eyeblink activity (56.8 vs 58.5 mm).

For the 60 subjects, the conjunctival tactile threshold was much lower than the corneal threshold, with the group mean value for the just detectable filament length being $26.2\pm$ 4.5 mm (p < 0.001 compared to central cornea). There was a relatively wide spread of conjunctival sensitivity values and, as shown in Fig. 4, a rather pronounced inverse relationship between the conjunctival sensitivity and SEBR, i.e. the lower the conjunctival sensitivity (shorter filament lengths needed to produce a just detectable sensation), the higher the expected SEBR. Overall, this association was highly statistically significant (p < 0.001, r = 0.588) and, very importantly, this effect was still seen if the group with frequent eyeblink activity were analysed separately (p < 0.001, r =0.530). The differences in ether corneal (not shown) or conjunctival tactile sensitivity (Fig. 5) were not obviously related to the exposed ocular surface area. Correlation analyses revealed no statistically significant interdependence $(p \ge 0.5, \text{Pearson } r \text{ value} = 0.076, \text{Spearman } r_s = 0.082).$

Discussion

Our study reveals that there can be a substantial association between bulbar conjunctival tactile sensitivity and the spontaneous eyeblink rate in generally healthy individuals, i.e. the subjects in this study did not have any form of dryeye disease, keratoconjunctivitis sicca etc. It might be

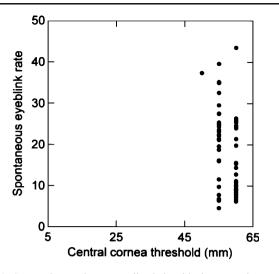


Fig. 3 Scatterplot to show overall relationship between the spontaneous eyeblink rate (in eyeblinks/min) and the central corneal tactile threshold for a mechanical stimulus (in mm)

argued that a significant limitation of our study was that only male subjects were assessed. This was largely a matter of cultural preference, although it has yet to be established in larger scale studies that healthy (older) women do have a consistent or predictable difference in spontaneous eyeblink rate or in the duration of their spontaneous eyeblink events, regardless of age [7, 9, 13, 28, 31, 32] (see later). Notwithstanding, the results from our study provide an important clue as to the nature of the control of spontaneous eyeblink activity, and perhaps why a substantial correlation has not been found between ocular symptoms and spontaneous eyeblink activity in essentially normal and healthy individuals. The reasons why such a remarkable

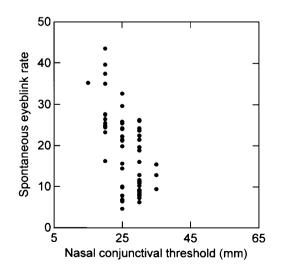


Fig. 4 Scatterplot to show overall relationship between the spontaneous eyeblink rate (in eyeblinks/min) and the conjunctival tactile threshold for a mechanical stimulus (in mm)

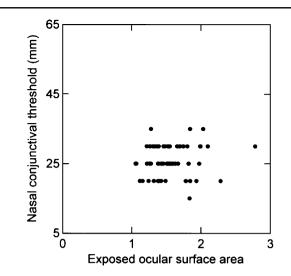


Fig. 5 Scatterplot to show the lack of any relationship between the exposed ocular surface area (in cm^2) and the conjunctival tactile threshold for a mechanical stimulus (in mm)

effect has not perhaps been observed before is perhaps the result of three inter-related issues. These issues relate to a possible confusion between symptoms and ocular surface sensitivity, the type of subjects assessed, and lastly to limitations of the method used to assess sensitivity.

Our study confirms and extends those made on elderly individuals (of either gender), in that there is no obvious relationship between the exposed ocular surface area in primary gaze and spontaneous eyeblink activity [9]. As with the present cohort, these elderly individuals did not have substantial symptoms, at least when assessed in a neutral environment. This is where some confusion may arise between symptoms and ocular surface sensitivity as measured with an exogeneous (external) stimulus. Intuitively, an increase in eyeblink rate would be expected if there is some form of exogenous stimulus to some aspect of the ocular surface that would probably be considered to be irritating in nature. As an example, increased blink rate values have been reported when the face and eye of human subjects are exposed to drafts of air [13, 14, 22] and this has been linked to an enhanced sensitivity (hyperesthesia) to an air jet stimulus to the ocular surface [33]. However, this is somewhat different to a more general consideration that those with chronic dry-eye disease would perhaps be more likely to report symptoms of ocular discomfort, and that the higher level of symptoms would be linked to increased eyeblink activity [13, 22]. The level of perceived symptoms is more a form of endogenous control or internal stimulus.

Our study, on a group of essentially healthy adult male subjects, is presented to illustrate that higher SEBR values (i.e. frequent eyeblink activity) can be associated with a marked difference in conjunctival tactile sensitivity to a nylon filament stimulus. Our subjects, especially those with

frequent eyeblink activity, did not report a higher level of symptoms and, in fact, their averaged symptom scores were marginally lower than those with what was considered to be normal spontaneous eyeblink activity. The difference in reported symptoms between the groups was however very small, and not statistically significant. At low levels, therefore, symptoms are not obviously correlated with SEBR. Our study is, however, limited to an assessment of the instantaneous tactile sensitivity, which is all that can really be delivered with such a simple filament-based mechanical stimulus. However, it would be useful to know if there are differences in the stimulus intensity versus duration of a tactile stimulus [34, 35], especially when comparing those with normal and frequent eyeblink activity. It would also be useful to further assess whether the change in eyeblink activity to other types of external stimuli such as drafts of air could be linked to the exposed ocular surface, i.e. reflecting the total sum of stimulation of trigeminal receptors. Such possible differences in sensitivity of the exposed ocular surface could be a very relevant factor in determining ocular comfort in specific activities such as VDU work [36, 37].

Our findings are not in contradiction to a general idea that an increased SEBR can result from an exogenous stimulus (that will trigger eyelid closure). However, our findings indicate that the endogenous signals from the ocular surface may serve to not only trigger eyelid closure (e.g. a sharp pain and blepharospasm in cases of exposure keratopathy or recurrent corneal erosion [38]), but could also serve as the natural inhibitory pathway to reduce or stop enhanced blink rates. Such a difference in ocular surface sensitivity could be linked to the actual control of spontaneous eyeblink activity by a trigeminal input [39, 40], specifically that controlling inhibition of eyeblinking [41]. Stated another way, a high conjunctival sensitivity (low threshold) would appear to be required to keep the overall SEBR at lower values. The same circuits may also be linked to tonic inhibitory cells in the pons, i.e. a subcortical feedback loop [6]. It is proposed that this system could work as a negative feedback, i.e. the greater the sensitivity (i.e. the lower the tactile threshold), the greater the inhibitory influence exerted on the eyeblink induction or the repeat of an eyeblink. The natural point of mechanical (tactile) contact for the bulbar conjunctiva would presumably be with the eyelid marginal zone in primary eye gaze. If the eyegaze was directed inferiorly, then that lid margin contact would now be with the cornea, and the sensitivity of the feedback control and thus the SEBR would be expected to be different [7]. Such neural pathways for eyeblink control may also be those altered in the elderly, who can show a form of frequent eyeblink activity [9, 39] referred to as 'reflexive blinking' [39]. With some recent studies concluding that frequent eyeblink

activity may be specifically found in older women [11], it would be useful to undertake further studies on ocular surface sensitivity in this particular group of individuals.

In the present group of subjects, those with a marginally lower value for corneal tactile sensitivity showed slightly higher eyeblink rates. The difference was small for these generally normal subjects, but the effect is consistent with reports that reduced tactile sensitivity (corneal hypoaesthesia) could be associated with increased eyeblink rates in those with dry-eye disease, e.g. KCS or Sjögren's syndrome [42, 43]. The Cochet-Bonnet aesthesiometer has, however, a limitation, in that even at maximum extension of the 0.12-mm diameter filament, it is possible that the stimulus delivered is still a suprathreshold one. A more obvious inter-relationship between corneal tactile sensitivity and SEBR might be observable if the true tactile threshold could be established. For example, if some of those thought to have a threshold of 60 mm could be shown to actually be able to detect a lesser stimulus (e.g. a '65'-mm filament length) and also have very low SEBR values, then a more obvious relationship might be apparent between corneal tactile sensitivity and spontaneous eveblink rate. This is not practically possible, but is logical, since there is such a notable inverse relationship between the tactile sensitivity of the bulbar conjunctiva and the SEBR value that was later calculated for each subject when their video recordings were analysed. These video analyses routinely took place several days after the recordings were made, i.e. the assessment of the tactile sensitivity was done without the subject or the investigators knowing that the subject had been assigned to a particular eyeblink group. With the range of sensitivities noted for the bulbar conjunctiva, there is no obvious limitation to the use of the aesthesiometer. Every effort was made to present the filament perpendicularly to the bulbar conjunctival surface and in a consistent position. The tactile sensitivity measures were deliberately made on part of the habitually exposed bulbar conjunctiva. It should also be noted that all subjects had palpebral aperture anatomical characteristics that appeared to be within normal limits, i.e. none of them had obvious abnormalities that could mean that they had higher exposed ocular surface area, and so perhaps be supersensitive to extraneous stimuli.

In very general terms, spontaneous eyeblink activity can be considered to have both endogenous and exogeneous control [7]. The former has been more recently referred to as an eyeblink (control) center [44], although it has long been accepted that the triggering of spontaneous eyeblink activity has some form of endogenous control, principally involving the frontal striate cortex [1–3, 6, 45]. In general, there appears to be a need to further investigate the interactions between eyeblink control pathways. There may be interde-

pendencies that need to be considered and addressed in the design of experimental studies. For example, it was recently noted that a possible difference in the outcome between studies investigating the role of complex and dynamic visual inputs on spontaneous eyeblink activity could be due to the differences in the baseline eyeblink rate of subjects [46]. Our study is presented as evidence that there could be a subtle neurological difference between subjects with frequent versus normal eyeblink activity, and that this seems to be rather different from any previously considered central integration of neural pathways.

From a practical perspective, beyond actually measuring the conjunctival tactile sensitivity, it is suggested that attention be given to the so-called baseline SEBR values in subjects being recruited for any type of eyeblink studies [7]. The main reason for classification of subjects as exhibiting normal versus frequent SEBR values represents the upper limit of values more commonly reported by different investigators for presumably normal individuals when the eyeblinking was recorded in primary gaze [7], although the concept of this cut-off has been supported by a retrospective analysis of the SEBR in 100 subjects with a wide range of ages [31]. In addition, more detailed information should be routinely provided about the environment under which studies are undertaken, and the status of the subject during eyeblink recording be clearly described. For example, if one were asking an individual to concentrate on and respond to a simple visual stimulus presented on a monitor directly in front of them in primary eye position, it would probably be argued that this task should be undertaken in silence. Providing the visual information was not too complex or dynamic, the eyeblink rate would be expected to be fairly low. If the subject was then asked to respond from this 'baseline' situation to a changed visual stimulus and/or increased level of thinking about or responding to the altered visual stimulus, then it should be fairly easy to observe an increase in eyeblink rate, partly because the baseline rates were relatively low. However, if the task were being undertaken with the subject engaged in conversation and/or provided with other distractions, it might be more difficult to observe a predictable increase in eyeblink rate associated with increased levels of visual processing, simply because the baseline eyeblink rate was already high.

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References

 Ponder E, Kennedy WP (1927) On the act of blinking. Q J Exp Physiol 18:89–110

- Stern JA, Walrath LC, Goldstein R (1984) The endogenous eyeblink. Psychobiol 21:22–33
- Karson CN (1988) Physiology of normal and abnormal blinking. Adv Neurol 49:25–37
- Vreugdenhil H, Brouwers P, Wolters P, Bakker D, Moss H (1997) Spontaneous eye blinking, a measure of dopaminergic function, in children with acquired immunodeficiency syndrome. Arch Pediatr Adolesc Med 151:1025–1032
- Tsubota K, Kwong KK, Lee T-Y, Nakamura J, Cheng H-M (1999) Functional MRI of brain activation by eye blinking. Exp Eye Res 69:1–7. doi:10.1006/exer.1999.0660
- Bour LJ, Aramideh M, Ongerboer de Visser BW (2000) Neurophysiological aspects of eye and eyelid movements during blinking in humans. J Neurophysiol 83:166–176
- Doughty MJ (2001) Consideration of three types of spontaneous eyeblink activity in normal humans: during reading and video display terminal use, in primary gaze, and while in conversation. Optom Vis Sci 78:712–725. doi:10.1097/00006324-200110000-00011
- Bentivoglio AR, Bressman SB, Cassetta E, Carretta D, Tonali P, Albanese A (1997) Analysis of blink rate patterns in normal subjects. Mov Disord 12:1028–1034. doi:10.1002/ mds.870120629
- Zaman ML, Doughty MJ, Button NF (1999) The exposed ocular surface and its relationship to spontaneous eyeblink rate in elderly Caucasians. Exp Eye Res 67:681–686. doi:10.1006/ exer.1998.0571
- Mori A, Egami F, Nakamori K, Ohtsuki T, Aikawa K, Shintani M, Matsumoto Y, Goto E, Tsubota K (2008) Quantitative videographic analysis of blink patterns of newscasters. Graefes Arch Clin Exp Ophthalmol 246:1449–1453. doi:10.1007/s00417-008-0887-3
- Sforza C, Rango M, Galante D, Bresolin N, Ferrario VF (2008) Spontaneous blinking in healthy persons: an optokinetic study of eyelid motion. Ophthalmic Physiol Opt 28:345–353. doi:10.1111/ j.1475-1313.2008.00577.x
- 12. Kleno J, Wolkoff P (2004) Changes in eye blink frequency as a measure of trigeminal stimulation by exposure to limonene oxidation products, isoprene oxidation products and nitrate radicals. Int Arch Occup Environ Health 77:235–243. doi:10.1007/s00420-003-0502-1
- Tsubota K, Hara S, Okusawa Y, Egami F, Ohtsuki T, Nakamori K (1996) Quantitative videographic analysis of blinking in normal subjects and patients with dry eye. Arch Ophthalmol 114:715–720
- Acosta MC, Gallar J, Belmonte C (1999) The influence of eye solutions on blinking and ocular comfort at rest and during work at a video display terminals. Exp Eye Res 68:663–669. doi:10.1006/exer.1998.0656
- Walker JC, Kendal-Reed M, Utell MJ, Cain WS (2001) Human breathing and eye blink rate responses to airborne chemicals. Environ Health Perspect 109(suppl 4):507–512. doi:10.2307/ 3454661
- Wolkoff P, Nojgaard JK, Toiano P, Picoli B (2005) Eye complaints in the office environment: precorneal tear film integrity influenced by eye blinking frequency. Occup Environ Med 62:4–12. doi:10.1136/oem.2004.016030
- 17. Kugelberg E (1952) Facial reflexes. Brain 75:385–396. doi:10.1093/brain/75.3.385
- Millodot M (1973) Objective measurement of corneal sensitivity. Acta Ophthalmol (Copenh) 51:325–334
- Gallar J, Acosta MC, Gutiérrez AR, Belmonte C (2007) Impulse activity in corneal sensory nerve fibers after photorefractive keratectomy. Invest Ophthalmol Vis Sci 48:4033–4037. doi:10.1167/iovs.07-0012
- Huber P (1962) Untersuchungen über die Beeinflussung des spontanen Lidschlages durch Lokal-Anaesthetica. Graefes Arch Clin Exp Ophthalmol (forerunner) 164:594–611. doi:10.1007/ BF00682809

- 21. Collins M, Seeto R, Campbell L, Ross M (1989) Blinking and corneal sensitivity. Acta Ophthalmol (Copenh) 67:525–531
- Nakamori K, Odawara M, Nakajima T, Mizutani T, Tsubota K (1997) Blinking is controlled primarily by ocular surface conditions. Am J Ophthalmol 124:24–30
- Fruedenthaler N, Neuf H, Kadner G, Schlote T (2003) Characteristics of spontaneous eyeblink activity during video display terminal use in healthy volunteers. Graefes Arch Clin Exp Ophthalmol 241:914–920. doi:10.1007/s00417-003-0786-6
- Naase T, Doughty MJ, Button NF (2005) An assessment of the pattern of spontaneous eyeblink activity under the influence of topical ocular anaesthesia. Graefes Arch Clin Exp Ophthalmol 243:306–312. doi:10.1007/s00417-004-0990-z
- Barbarato G, Ficca G, Muscettola G, Fichele M, Beatrice M, Rinaldi F (2000) Diurnal variation in spontaneous eye-blink rate. Psychiatry Res 93:145–151. doi:10.1016/S0165-1781(00)00108-6
- 26. Doughty MJ, Blades KA, Ibrahim N (2002) Assessment of the number of eye symptoms and the impact of some confounding variable for office staff in non-air-conditioned buildings. Ophthalmic Physiol Opt 22:143–155. doi:10.1046/j.1475-1313.2002.00013.x
- Zaman ML, Doughty MJ (1997) Some methodological issues in the assessment of the spontaneous eyeblink in man. Ophthalmic Physiol Opt 17:421–432
- Doughty MJ (2002) Further assessment of gender- and blink pattern-related differences in the spontaneous eyeblink activity in primary gaze in young adult humans. Optom Vis Sci 79:439–447. doi:10.1097/00006324-200207000-00013
- 29. Cochet P, Bonnet R (1960) L'esthésie cornéene. Sa mesure clinique. Clin Ophtalmol 4:3–27
- Terry RL, Schnider CM, Holden BA, Cornish R, Grant T, Sweeney D, La Hood D, Back A (1993) CCLRU standards for success of daily and extended wear contact lenses. Optom Vis Sci 70:234–243. doi:10.1097/00006324-199303000-00011
- 31. Doughty MJ, Naase T (2006) Further analysis of the human spontaneous eyeblink rate by a cluster analysis-based approach to categorize individuals with 'normal' versus 'frequent' eye blink activity. Eye Contact Lens 32:294–299. doi:10.1097/01. icl.0000224359.32709.4d
- 32. Schellini A, Sampaio AA, Hoyama E, Cruz AAV, Padovani CR (2005) Spontaneous eye blink analysis in the normal individual. Orbit 24:239–242. doi:10.1080/01676830590922057
- De Pavia CS, Pflugfelder SC (2004) Corneal epitheliopathy of dry eye induces hyperesthesia to mechanical air jet stimulation. Am J Ophthalmol 137:109–115. doi:10.1016/S0002-9394(03)00897-3

- Jalavisto E, Orma E, Tawast M (1951) Ageing and relation between stimulus intensity and duration in corneal sensibility. Acta Physiol Scand 23:224–233. doi:10.1111/j.1748-1716.1951.tb00812.x
- Manning KA, Evinger C (1986) Different forms of blinks and their two-stage control. Exp Brain Res 64:579–588. doi:10.1007/ BF00340495
- 36. Helland M, Horgen G, Kvikstad TM, Garthus T, Bruenech JR, Aaras A (2008) Musculoskeletal, visual and psychsocial stress in VDU operators after moving to an ergonomically designed office landscape. Appl Ergon 39:284–295. doi:10.1016/j. apergo.2007.10.005
- 37. Aakre BM, Doughty MJ (2007) Are there differences between 'visual symptoms' and specific ocular symptoms associated with video display terminal (VDT) use? Cont Lens Anterior Eye 30:174–182. doi:10.1016/j.clae.2007.01.001
- McMonies CW (2007) Incomplete blinking: Exposure keratopathy, lid wiper epitheliopathy, dry eye, refractive surgery, and dry contact lenses. Cont Lens Anterior Eye 30:37–51. doi:10.1016/j. clae.2006.12.002
- Peshori KR, Schicatano EJ, Gopalaswamy R, Sahay E, Evinger C (2001) Aging of the trigmeninal blink system. Exp Brain Res 136:351–363. doi:10.1007/s002210000585
- Dimitrova A, Weber J, Maschke M, Elles H-G, Kolb FP, Forsting M, Diener H-C, Timmann D (2002) Eyeblink-related areas in human cerebellum shown by fMRI. Hum Brain Mapp 17:100–115. doi:10.1002/hbm.10056
- Powers AS, Schicatano EJ, Basso MA, Evinger C (1997) To blink or not to blink: inhibition and facilitation of reflex blinks. Exp Brain Res 113:283–290. doi:10.1007/BF02450326
- 42. Xu KP, Yagi Y, Tsubota K (1996) Decrease in corneal sensitivity and change in tear function in dry eye. Cornea 15:235–239. doi:10.1097/00003226-199605000-00002
- Bourcier T, Acosta MC, Borderie V, Borras F, Gallar J, Bury T, Laroche L, Belmonte C (2005) Decreased corneal sensitivity in patients with dry eye. Invest Ophthalmol Vis Sci 46:2341–2345. doi:10.1167/iovs.04-1426
- 44. Ongerboer de Visser BW, Bour LJ (2006) Eye and eyelid movements during blinking: an eye blink centre? Clin Neurophysiol 58(suppl):16–25
- Peterson J, Allison LW (1931) Controls of the eye-wink mechanism. J Exp Psychol 14:144–154. doi:10.1037/h0070197
- Colzato LS, van Wouwe NC, Hommel B (2007) Spontaneous eyeblink rate predicts the strength of visuomotor binding. Neuropsychologia 45:2387–2392. doi:10.1016/j.neuropsychologia.2007.03.004