Sleep Medicine Reviews 45 (2019) 95–104

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Narrative review: Do spontaneous eye blink parameters provide a useful assessment of state drowsiness?

Jennifer M. Cori [a, *], Clare Anderson [b], Shamsi Shekari Soleimanloo [a, b], Melinda L. Jackson [a, c], Mark E. Howard [a, b, d]

[a] Institute for Breathing and Sleep, Austin Health, Heidelberg, Victoria, Australia
[b] School of Psychological Sciences, Monash University, Clayton, Victoria, Australia
[c] School of Health & Biomedical Sciences, RMIT University, Bundoora, Victoria, Australia
[d] Department of Medicine, University of Melbourne, Parkville, Victoria, Australia

ARTICLE INFO

Article history:
Received 20 November 2018
Received in revised form
10 March 2019
Accepted 14 March 2019
Available online 20 March 2019

Keywords:
Eye blink
Eyelid
Ocular
Drowsiness
Sleepiness
Vigilance
Extended wakefulness
Circadian alertness
Obstructive sleep apnoea

SUMMARY

Most objective drowsiness measures have limited ability to provide continuous, accurate assessment of drowsiness state in operational settings. Spontaneous eye blink parameters are ideal for drowsiness assessment as they are objective, non-invasive, and can be recorded continuously during regular activities. Studies that have assessed the spontaneous eye blink as a drowsiness measure are diverse, varying greatly in respect to study design, eye blink acquisition technology and eye blink parameters assessed. The purpose of this narrative review is to collate these studies to determine 1) which eye blink parameters provide the best state drowsiness measures; 2) how well eye blink parameters relate to and predict conventional drowsiness measures and 3) whether eye blink parameters can identify drowsiness impairment in obstructive sleep apnoea (OSA) - a highly prevalent disorder associated with excessive sleepiness and increased accident risk. In summary, almost all eye blink parameters varied consistently with drowsiness state, with blink duration and percentage of eye closure the most robust. All eye blink parameters were associated with and predicted conventional drowsiness measures, with generally fair to good accuracy. Eye blink parameters also showed utility for identifying OSA patients and treatment response, suggesting these parameters may identify drowsiness impairment in this group.

Introduction

Drowsiness is a fluctuating, intermediate state between wakefulness and sleep, characterised by an uncontrollable propensity to sleep, slowed reactions, reduced attention and impaired neurobehavioral performance [1–3]. Motor vehicle drivers who show physical signs of drowsiness are three times more likely to have an accident than non-drowsy drivers [4]. The related health and economic impact is substantial, as drowsiness related motor vehicle accidents are likely to result in death and serious injury [5]. Drowsiness also affects occupational productivity, with individuals who suffer from sleep disorders more likely to make errors, as well as fall asleep at, and be absent from the workplace [6]. To minimise the health and economic burden of drowsiness, simple and accurate tools are required that objectively measure drowsiness.

Numerous subjective, behavioural and physiological measures of drowsiness exist, but each has limitations. Self-report measures such as the Karolinska sleepiness scale (KSS) [7] are simple to administer and while many individuals show an awareness of their sleepiness that is associated with objective outcomes [8–10] reporting may be unreliable in operational settings or under chronic levels of insufficient sleep [11]. Cognitive or psychomotor tasks also provide a simple drowsiness measure, but are disruptive to regular activities. In contrast, physiological indices such as ocular measures and electroencephalogram (EEG) can theoretically provide continuous drowsiness assessment during regular activities with minimal interruption. EEG is the most extensively studied physiological indicator of drowsiness and has good validity [12], however its routine use in the field is limited by challenges with signal noise, electrode application, and limited real-time analysis. Whereas technological advancements have enabled simple real-time analysis of eye blink parameters that is appropriate for use both in laboratory and in field.

* Corresponding author.
E-mail address: jmcori1989@gmail.com (J.M. Cori).

https://doi.org/10.1016/j.smrv.2019.03.004
1087-0792/

Abbreviations

-AVR	Negative amplitude-velocity ratio – Ratio of amplitude to velocity of the eyelid reopening phase
+AVR	Positive amplitude-velocity ratio - Ratio of amplitude to velocity of the eyelid closing phase
aMT6s	6-suplhatoxymelatonin
AUC	Area under the curve
BTD	Blink total duration
CBT	Core body temperature
CPAP	Continuous positive airway pressure
EEG	Electroencephalogram
EOG	Electrooculogram
IED	Inter-event duration – A blink duration measure
JDS	Johns drowsiness scale
KSS	Karolinska sleepiness scale
LEC	Long eye closures
MWT	Maintenance of wakefulness test
OSA	Obstructive sleep apnoea
OSLER	Oxford sleep resistance test
PERCLOS	Percentage of time with the eyes closed
PVT	Psychomotor vigilance test
TEC	Time with eyes closed
TIB	Time in bed

The spontaneous eye blink

The spontaneous eye blink is controlled by two opposing ocular muscles, the orbicularis oculi and the levator palpebrae. These muscles are innervated by the seventh and eighth cranial nerves, with nuclei located between the pons and medulla. The close proximity of these nuclei to the structures that control the sleep-wake state provides a neurophysiological basis as to why these eye blink parameters provide insight into drowsiness state.

Spontaneous eye blink parameters used to indicate drowsiness can be broadly grouped into measures of blink frequency, duration, percentage of time with the eyes closed, eyelid speed and composite measures (see Table 1 and Fig. 1). These parameters are typically averaged across one minute time windows. Electrooculogram (EOG) [13–30], digital video [28,31–36] and infrared oculography [3,29,31,37–45] have each been used for eye blink measurement (Fig. 1) and have different benefits and technical challenges. EOG utilises electrodes placed adjacent to the eyes and is highly accurate in detecting blinks due to a high sampling rate. However, real-time analysis has not been developed and electrode placement is impractical in operational scenarios with data loss frequent due to poor electrode contact or movement artefact. Digital video records images of the face and eyes, and typically uses feature detection software to extract relevant eye blink metrics. Digital video has the advantage of being non-obtrusive, but is suitable only for monitoring where the individual is stationary and the main direction of gaze is fixed, such as during driving. Digital video cannot detect parameters when the eyes are out of frame and can struggle with high light reflectance conditions or when sunglasses are worn, although technological advancements appear to be overcoming the latter issues [46]. Infrared oculography utilises an infrared sensor, typically embedded within or connected to a glasses frame, which extracts eye blink parameters by measuring eyelid position. Unlike digital video, infrared oculography is attached to the individual, which minimizes data loss, but movement artefact can impair signal quality, and some users may find wearing a device uncomfortable or undesirable. Furthermore, with infrared oculography, individual signal calibration is often required to obtain optimal signal quality because of interindividual differences in facial structure. Despite these limitations, digital video and infrared oculography have the advantage of providing real-time analysis suitable for use in ambulatory and/or operational

Table 1
Spontaneous eye blink parameters broadly categorised into measures of eye blink frequency, duration, eyelid speed, percentage of eye closure and composite measures. Definition of parameter and acquisition techniques used are also shown.

Category	Parameter	Definition	Acquisition Technique
Frequency	Eye blink rate	Eye blink rate during a specified time window (usually 1 min)	EOG [13,14,23–29] Video [34–36] IO [38,42]
Duration	Total blink	Duration of the closing, closed and reopening phases of the blink eye blink	EOG [15–22,27,28,30] IO [3,29,37,39–42]
	Closed phase	The duration of the closed phase of an eye blink only	Video [34,36] EOG [28] IO [38,42]
	Closing phase	Eye blink closing phase duration only	EOG [28] IO [38,42]
	Reopening phase	Eye blink reopening phase duration only	EOG [28] IO [38,42]
	Inter-event duration (IED)	Time between the maximum velocity of the eyelid reopening to the maximum velocity of the eyelid closing	IO [3,37,41–43]
Eyelid speed	Negative Amplitude-Velocity Ratio (-AVR)	Ratio of eyelid reopening amplitude to velocity	IO [3,39–41,43] EOG [27,28]
	Positive Amplitude-Velocity Ratio (+AVR)	Ratio of eyelid closing amplitude to velocity	IO [37,39–41] EOG [27,28]
Percentage of eye closure	Percentage of time with the eyes closed (PERCLOS)	Percentage of time the eyes are closed (usually defined as >80% of pupil coverage in 5 min)	Video [28,31–33]
	% Time eyes closed (TEC)	Percentage of time per minute that the eyelids are deemed to be closed	IO [3,29,31,37,39–41]
	% Long eye closures (LEC)	Percentage of time per minute that the eyelids are deemed to be closed for longer than 10 ms	IO [3,29,38,42,43]
Composite measure	Johns Drowsiness Scales (JDS)	Scaled from 0 (very alert) to 10 (very drowsy)	IO [3,9,29,31,37,39–41,44]
	Photooculography	Scaled from 0 (well alert) to 10 (very drowsy)	Photo [50]

Legend: EOG – Electrooculogram; IO – Infrared oculography.

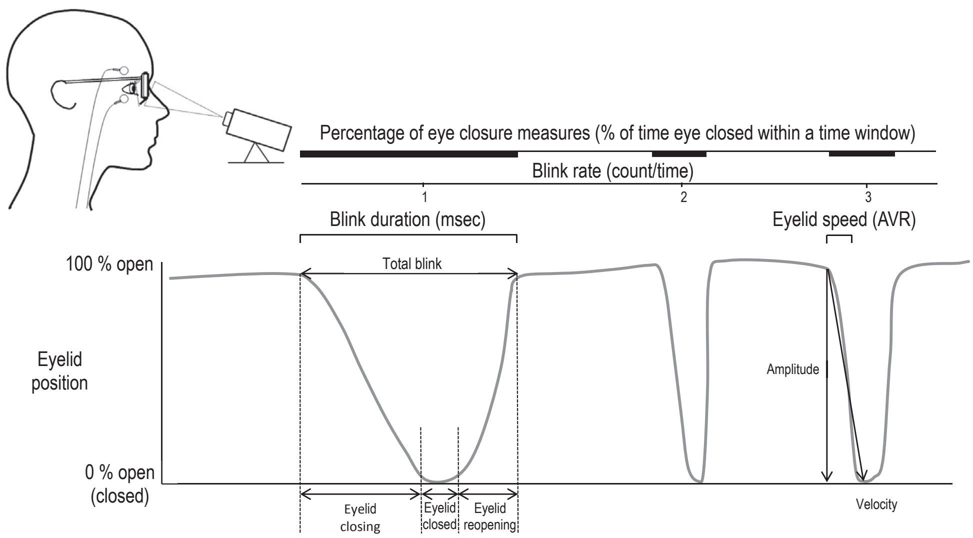

Fig. 1. Top left contains an example schematic of eye blink acquisition technologies – video camera, infrared sensor (attached to glasses frames) and electrooculogram ([EOG] – electrodes around the eyes). Below this is a schematic of key eyeblink parameters attained by these technologies: blink duration, eyelid speed, blink rate and percentage of eye closure measures. Note composite measures can also be attained by combining multiple measures. AVR- Amplitude velocity ratio.

environments. Proprietary devices that utilise these measures typically have in-built alarm systems that can notify the user if they are close to, or have exceeded, critical drowsiness levels, enabling the user to intervene to mitigate the drowsiness risk. A further advantage of these devices is that they have the capability to transmit acquired drowsiness information in real-time to operational command centres, giving the employers the potential to monitor their employees' drowsiness state and intervene as appropriate.

The digital video and infrared oculography eye blink proprietary drowsiness monitoring devices work by filtering eye blink parameters through black box algorithms to produce a score that is then compared to a drowsiness cut-off value. For example, Optalert, which utilises infrared oculography, calculates the John's Drowsiness Scale (JDS), a composite measure that includes parameters of eye blink amplitude-velocity ratios and blink durations [44,47]. JDS scores vary between 0-very alert, and 10-very drowsy, with values updated every minute. Scores between 4.5 and 4.9 signal a cautionary warning, while scores greater than five signal a critical warning [47]. A description and evaluation of other proprietary ocular drowsiness monitoring devices, that have only had limited empirical validation are provided elsewhere [12].

Given that eye blink measures of drowsiness have been assessed using diverse study designs and a variety of recording techniques, the purpose of this review was to collate the literature to evaluate: 1) Which eye blink parameters provide the most useful measure of state drowsiness; 2) How different eye blink parameters compare to existing drowsiness measures and 3) How useful eye blink parameters are for detecting drowsiness in patients affected by obstructive sleep apnoea (OSA) – a highly prevalent sleep disorder associated with fragmented sleep, excessive daytime sleepiness and increased motor vehicle accident risk.

To ensure relevant empirical work was considered a search strategy was used that identified articles that had assessed eye blink parameters during drowsiness inducing conditions of extended wakefulness/restricted sleep, low circadian alertness and OSA. For a detailed description of the search see the online supplement.

Section 1 - Which eye blink parameters provide the most useful measure of state drowsiness?

To be a useful measure, eye blink parameters must vary in a predictable direction with drowsiness state. Studies that measured eye blink parameters during alert and drowsy conditions were reviewed in relation to the drowsiness inducing condition assessed (extended wakefulness/restricted sleep and low circadian alertness) and are listed in Table 2. Because the tasks during which eye blink parameters were recorded varied, and tasks that are more simple and mundane have a greater impact on drowsiness [48], studies were further categorised according to task complexity.

Extended wakefulness

Minimal complexity and engagement tasks

Fixation tasks. Fixation tasks involve staring at a wall or computer screen for several minutes. EOG blink rate during fixation tasks has been assessed in several studies with conflicting results. In two studies, eye blink rate progressively increased across extended wakefulness, such that after ~24 h awake, values were up to twice that of baseline levels [13,14]. In contrast, a longer 32 h sleep deprivation study showed that while eye blink rate initially increased across the first 16 h, it then progressively declined across the last 16 h [23]. This discrepancy may be because in extreme drowsiness, eye blink rate dissipates as the amount of time spent with the eyes closed increases. This notion is supported by a study that utilised infrared oculography and demonstrated that at 30 h of extended wake there was 3–4 fold increase in eye closure metrics of percentage of time with the eyes closed (%TEC) and long eye closures (%LEC) as well as a doubling of blink total duration (BTD) from baseline [3]. However, blink rate was not assessed in this study. Other eye blink measures that were assessed, were the composite measure the JDS, which increased by 55% and the eyelid reopening amplitude to velocity ratio (-AVR) which increased by ~13%, indicating that these combination measures may be useful indicators of drowsiness state [3].

Table 2
Studies that have assessed eye blink parameters under drowsiness inducing conditions. Studies are organised according to drowsiness inducing condition: extended wakefulness and low circadian alertness, as well as task complexity and level of engagement required: Minimum, Moderate, High and Very High.

Condition	Task Type	Study	Participants	Male	Age range	Eye blink Frequency	Eye blink duration	Eye closure	Composite Measure	Eyelid closing speed	Eyelid Reopening Speed
				(%)	years)				JDS	(+AVR)	(−AVR)
Extended Wake	Min – FT	Anderson C et al 2013 [3]	H = 29	62	18–34		↑ IO	↑ IO	↑ IO		↑ IO
		Barbato G et al 1995 [13]	H = 8	25	N/A	↑ E					
		Barbato G et al 2007 [14]	H = 25	32	18–23	↑ E					
		Cajochen C et al 1999 [23]	H = 10	100	21–31	NC E					
	Mod – PVT	François C et al 2016 [50]	H = 24	46	19–34				↑ P ^		
		Ftouni S et al 2013 [39]	H = 10	100	20–25		NC IO	↑ IO	↑ IO	↑ IO	↑ IO
		Jackson ML et al 2016 [31]	H = 22	14	18–26			↑ IO & NC V	↑ IO		
		Jackson ML et al 2016 [32]	PD = 12	92	23–62			↑ V			
		Ong JL et al 2013 [49]	H = 19	59	18–35			↑ V			
	High – DS	Akerstedt T et al 2005 [30]	SW = 10	50	N/A		↑ E				
		Alvaro PK et al 2016 [33]	PD = 20	100	N/A			↑ V			
		Anund A et al 2009 [15]	H = 17	47	N/A		↑ E				
		Jackson ML et al 2016 [31]	H = 22	14	18–26			↑ IO & NC V	↑ IO		
		Jackson ML et al 2016 [32]	PD = 12	92	23–62			↑ V			
	Very High – DR	Anderson C et al 2018 [9]	SW = 16	38	25–33				↑IO		
		Ftouni S et al 2013 [29]	SW = 27	15	N/A		↑ IO	↑ IO	↑ IO		
		Lee ML et al 2016 [37]	SW = 16	44	19–65		↑ [a] IO	NC IO	↑ [a] IO	↑ [a] IO	
		Shiferaw BA et al 2018 [34]	H = 9	44	N/A	↑ V	↑ V				
Low circadian alertness	Min – FT	Anderson C et al 2013 [3]	H = 29	62	18–34		↑ IO	↑ IO	↑ IO		↑ IO
		Barbato G et al 2000 [24]	H = 24	33	18–23	↑ E					
		Caffier P et al 2003 [38]	H = 60	43	16–64	NC IO	↑ IO	↑ IO			
		De Padova V et al 2009 [25]	H = 12	25	64–79	NC E					
	High – DS	Ahlstrom C et al 2017 [19]	H = 30	100	18–25		↑ E				
		Ahlstrom C et al 2018 [21]	H = 30	100	18–25		↑ E				
		Anund A et al 2018 [20]	PD =11 & H =15	100	19–25		↑ E				
	Very High – DR	Akerstedt T et al 2013 [17]	H = 18	56	30–60		↑ E				
		Anund A et al 2013 [18]	H = 24	50	25–65		↑ E				
		Hallvig D et al 2014 [22]	H = 33	N/A	30–60		↑ E				
		Sandberg D et al 2011 [16]	H = 18	50	25–60		↑ E				
Extended wake X Low circadian alertness	Min – FT	Slama H et al 2018 [35]	H = 35	48	18–26	↑ V[a]					
	Mod – PVT	Ftouni S et al 2015 [40]	SW = 22	68	18–64		[a] IO	[a] IO	[a] IO	↑ [a] IO	NC IO

Task type refers to whether it is minimum (min), moderate (mod), high or very high level of engagement and complexity. FT - fixation task, PVT-Psychomotor Vigilance Test, DS- Driving simulation and DR- Driving on road. Participants refers to type of participant with H – Healthy, PD – Professional Driver and SW – Shift worker. The number after the = indicates how many participants were assessed. Recording technology is indicated by E for EOG, IO for Infrared oculography, V for Video and P for Photooculography. ↑ Indicates eye blink parameter significantly increased as a function of drowsiness condition, ↓ eyeblink parameter significantly decreased as a function of drowsiness condition, NC – no change in the parameter.

[a] Interaction effect of drowsiness condition and another measured parameter (such as time on task). JDS – Johns Drowsiness Score. ^ Indicates the one composite measure study that did not use the JDS.

Moderate complexity and engagement tasks

Psychomotor vigilance test. Eye blink parameters have also been measured during the psychomotor vigilance test (PVT), a simple reaction time task highly sensitive to sleepiness [11]. Following ~24 h of wakefulness, reaction times slowed and lapses increased relative to normal sleep or the first 16 h of wakefulness [31,32,39,49]. Eye closure metrics of %TEC and the percentage of time where >80% of the pupil is covered (PERCLOS) typically increased two- to three-fold following extended wakefulness [31,32,39,49]. Eyelid closing and opening speed slowed as indicated by a 20–30% increase in the amplitude-velocity ratios of the eyelids reopening (-AVR) and closing (+AVR). The composite measure the JDS increased by ~40–50% [31,39], while another composite measure based on photooculography (high speed camera images) increased by ~50% [50]. Blink duration, was the only parameter that did not show a significant time awake effect, with an initial increase and peak at ~24 h of wakefulness, followed by a decline in the subsequent 16 h [39]. This was possibly due to circadian effects, as the decline occurred between 0800 and 1600 h, when alertness levels were relatively high.

High complexity and engagement tasks

Simulated driving studies. Following extended wakefulness, simulated driving was associated with greater lane position and speed variability, slowed braking reaction times, and increased lane crossings and crash occurrence [15,30–32]. In respect to eye blink parameters, EOG blink duration increased by ~20% [15,30] and JDS increased by ~80% [31]. Eye closure metrics also worsened with an 11-fold increase in %TEC [31] and a three to five-fold increase in PERCLOS [31,32]; although the latter did not reach significance for one study [31]. The null finding may be explained by the recording technology, as a proprietary video device (Co-Pilot– no longer in production) was used to extract PERCLOS. This technology is restricted by direction of gaze and also a low sampling rate of 3 times per second, which was likely not enough to accurately detect eye closure. This is supported by the same study finding significant results for a similar measure (%TEC) [31] that was recorded simultaneously using infrared oculography, which sampled data at 500 times per second and has better tolerance to changes in gaze direction. This highlights the potential for different outcomes depending on acquisition technique.

Changes in the duration of single PERCLOS episodes (>1s) have also been examined across 24 h of wakefulness. In the first 14 h, episodes were infrequent and short in duration (1–3s), but after 17 h awake, 4–6s durations became prominent. After 23 h awake, eye closure durations up to 18s were observed [33]. Thus, the duration of individual eye closure episodes may be as useful for detecting drowsiness impairment as averaged metrics.

Very high complexity and engagement tasks

On road driving studies. Eye blink parameters have also been evaluated during on road driving. Following a night of no sleep, healthy individuals had a 3-fold increase in lane departure rate during a 2 h track drive relative to a night of regular sleep (7.7 ± 0.5 h) [34]. Eye blink rate and duration were also impaired following no sleep, increasing by 33% and 12% respectively [34]. Lee [37] similarly assessed shift workers following regular sleep and nightshift (where 7.6 ± 2.4 h and 0.4 ± 1.1 h of sleep was obtained respectively). Lane departure rate and near crashes were greater post nightshift. For eye blink parameters attained via infrared oculography, the JDS almost doubled and blink duration, measured by the time between the maximum velocity of the eyelid reopening to closing (inter-event duration [IED]), increased by 20%. Other parameters of blink duration (BTD) and eyelid closing speed (+AVR) varied with drive duration, but demonstrated a more rapid deterioration across the post nightshift drive. %TEC showed no effects relating to sleep condition but this may have been because drowsiness impairment was not extreme as participants had only been awake for 12.8 ± 4.8 h since their last sleep episode prior to the post nightshift drive.

Ftouni [29] assessed eye blink parameters in shift workers via infrared oculography during their regular commute to and from night shift across two weeks. Self-rated adverse driving events relating to sleep, inattention and hazard were greater post nightshift which was associated with an average of 15.8 ± 3.3 h of prior wakefulness. Eye blink parameters were also worse post-nightshift, with eye closure metrics of %LEC and %TEC increasing three and two-fold respectively. Blink duration as measured by BTD increased by 15% and the JDS increased by 22%. A similar study assessed medical physicians driving to and from six extended duration work shifts (28.3 ± 1.9 h in duration) [9]. Driving from shift was associated with a three to five-fold increase in self-reported adverse events relating to sleep, inattention, hazard and violations, as well as a 48% increase in JDS compared to the drive to shift. Therefore, these measures appear highly capable of detecting drowsiness in the real world during regular driving.

Low circadian alertness

Minimal complexity and engagement tasks

Fixation tasks. Time of day (a surrogate measure of circadian alertness) and its impact on EOG eye blink frequency has been assessed using fixation tasks spaced across regular waking hours [24,25]. One study demonstrated a 45% increase in blink rate when assessed in the evening (~20:30 h) relative to daytime, indicating potential circadian affects [24]. Whereas another study demonstrated no variation across sessions [25]. The inconsistent results may be related to eye blink frequency not being a consistent drowsiness indicator, or possibly, large differences in sample demographics between the two studies.

Time of day effects on eye blink parameters measured by infrared oculography were assessed during a fixation task in healthy participants in the morning before work, where it was assumed they were alert, and in the evening after work, where it was assumed they were drowsy [38]. Compared to the morning session, in the evening session the % of long closure duration blinks increased 3-fold. In addition, blink duration increased by 27%, eyelid reopening time increased by 34% and eyelid closing time increased by 13%. Blink rate was the only parameter to show no significant change.

Another study assessed the impact of circadian rhythm on eye blink parameters by assessing core body temperature (CBT) via a rectal thermometer during a 30 h extended wakefulness study [3]. Eye blink parameters were compared between low circadian alertness (the ‘biological night’ defined as 6 h before and 2 h after CBT minimum) and relatively high circadian alertness (average of 8 h prior to CBT maximum). During low circadian alertness, %TEC and %LEC approximately doubled and blink duration measures of BTD and IED increased by 39% and 23% respectively. Additionally, the composite measure the JDS increased by 45% and the amplitude to velocity ratio of eyelid reopening (-AVR) increased by 14%. Based on these findings, eye blink parameters appear to approximate circadian variations in alertness well.

High and very high complexity and engagement tasks

Simulated and on road driving studies. Time of day effects are also observed for simulated and on road driving performance, with night driving associated with greater lane position variability [16–18], increased line crossings [17,19–22] and reduced speed [16,17,19–21]. For eye blink parameters, EOG eye blink durations are longer during night driving [16–22] with an additional compounding interaction effect of drive duration [18,20,21].

Extended wakefulness and low circadian alertness

Minimal complexity and engagement tasks

Fixation tasks. Slama [35] assessed time of day effects on video eye blink rate during a fixation task in healthy individuals exposed to either normal sleep (397 ± 40 min) or no sleep. Eye blink rate approximately doubled in the extended wakefulness group from the evening to morning session, whereas there was no change in the normal sleep group.

Moderate complexity and engagement tasks

Psychomotor Vigilance Test. Ftouni [40] assessed extended wakefulness and circadian effects on eye blink parameters during the PVT. Shift workers were assessed at the beginning (20:00 h) and end of a simulated night shift (05:55 h), where they had spent ~16 h awake. Circadian phase was measured via a urinary metabolite of melatonin (6-suplhatoxymelatonin – aMT6s). At end shift, participants 3 h within the aMT6s acrophase had slower reaction times and an ~11-fold increase in eye closure (%TEC), an approximate doubling of the JDS and blink duration (BTD) measures, as well as an ~25% increase in +AVR compared to the beginning of the shift. In contrast, there was no or minimal change in eye blink parameters for participants 3 h outside of the aMT6s acrophase, thus reinforcing the circadian influence on these parameters. However, −AVR showed no effect, suggesting that it may be a less sensitive marker of circadian influences and extended wakefulness combined.

Summary

Blink duration and percentage of eye closure metrics were the most frequently evaluated eye blink parameters across studies and were shown to consistently increase irrespective of drowsiness condition, assessment tasks or acquisition technology, suggesting that they are robust state drowsiness measures (Table 2). The magnitude of the increase across experimental studies was typically between 10 and 40% for blink duration and two to four-fold for percentage of eye closure metrics. Blink duration had the advantage of also extensively being evaluated under low circadian alertness as well as high complexity tasks such as real on road driving. In contrast, percentage of eye closure metrics were mostly evaluated in the laboratory under conditions of extended wakefulness, and therefore during a more extreme drowsiness state. Whether percentage of eye closure metrics remain a good indicator of drowsiness in less extreme drowsiness states remains to be assessed. The JDS was the next most frequently studied parameter and also consistently increased during drowsiness, while eyelid closing and reopening speeds also showed promise. However, further work is required to determine the effect of circadian alertness on both of these parameters. Eye blink rate was the least consistent metric and while it mostly increased with drowsiness, some studies showed no change or a decrease, which may be due to a biphasic influence of drowsiness on this parameter. Notably restricted sleep effects were only assessed in two studies, but the direction of eye blink parameters was not clearly described for one study [27] and the other assessed eye blink parameters while the participants were trying to fall asleep [26] which may confound results. Thus, further studies evaluating how sleep restriction influences these eye blink parameters are required.

Section 2 – How well do spontaneous eye blink parameters compare to conventional drowsiness measures?

Eye blink measures have been related to existing drowsiness measures of subjective sleepiness, neurobehavioral performance, EEG and driving performance, validating their use for evaluation of drowsiness.

Subjective sleepiness

The relationship between eye blink parameters and subjective sleepiness has typically been assessed using the KSS, but also via visual analogue scale measures of drowsiness, with correlations generally ranging from moderate to strong [31,33,38,39], with some minimal or null findings also observed [17,18,35]. Laboratory studies have assessed the ability for eye blink parameters to predict the KSS. An extended wakefulness study assessed whether eye blink parameters derived from infrared oculography could predict KSS levels ≥ “some signs of sleepiness” using receiver operating characteristic area under the curve (AUC) analysis [3]. The ability of the predictor to detect drowsiness using AUC can be interpreted as: .90-.99 excellent, .80-.89 good, .70-.79 fair, .60-.69 poor and .59 or less fail [51]. JDS was shown to be a good predictor (AUC = .80), eye closure metrics fair (AUC = .76-.77), blink duration metrics poor to fair (AUC = .68-.71), and eyelid reopening speed poor (AUC = .68) [3]. Another laboratory study modelled the relationship between PERCLOS and KSS, but found no relationship (p = .32), although measurement was made using the aforementioned Co-Pilot device which had a low sampling rate [32]. An on road driving study supported the ability for eye blink parameters to approximate subjective sleepiness, as EOG blink duration while driving was a significant predictor of reported KSS while driving (regression slope = 0.006 and standard error = 0.000) [16].

Neurobehavioral performance

Psychomotor vigilance test

Numerous studies have shown that eye blink parameters moderately to strongly correlate with PVT lapses and reaction times [31,33,39,49,50]. Following extended wakefulness PERCLOS was demonstrated to be a strong predictor of lapses (r = .68) [32]. A similar metric %TEC was shown to be good at detecting ≥8 PVT lapses (AUC = 0.87) following extended wakefulness, which was equivalent to the number of lapses that occurred in the same participants at a blood alcohol content of 0.05% [31]. Other extended wakefulness studies assessed the ability for eye blink parameters measured via infrared oculography to detect a 50% and 75% increase in PVT lapses [3,39]. Eye blink parameters of JDS, BTD, %TEC and eyelid opening/closing speeds had poor to good detection ability, with JDS the best in one study (AUC = .74) [3], and +AVR the best in another (AUC = .82) [39]. For the latter study, +AVR was a better predictor of lapses than the KSS [39], suggesting a potential advantage of these metrics over conventional subjective drowsiness measures.

Oxford sleepiness resistance test

The Oxford sleepiness resistance test (OSLER) requires participants to continuously respond to stimuli presented at 3s intervals for 40 min [52]. For detecting at least one 1 OSLER lapse per minute following sleep restriction PERCLOS was good (AUC = .85), blink frequency fair (AUC = .79) and blink duration poor (AUC = .65) [28]. In contrast, a similar study found that blink duration best detected ≥4 consecutive OSLER lapses (AUC = .82), while eye closure metrics, the JDS, and eyelid closing/reopening speeds ranged between fail to fair (AUC = .58-.74) [41]. Differences in eye blink duration detection abilities between these studies may be related to differences in acquisition technology as the first utilised EOG and the latter infrared oculography, as well as differences in detection of different levels of drowsiness impairment (e.g., ≥1 lapse vs. ≥4).

Electroencephalogram

Few studies demonstrated moderate to strong correlations between eye blink parameters and EEG power spectra or EEG signs of sleepiness [13,17,39,50]. Eye blink parameters lag behind EEG power spectra by ~1 h [39]. However, the extent to which this corresponds to EEG-defined microsleeps is unknown.

Driving performance

Simulated driving

Moderate to strong correlations have been identified between eye blink metrics and simulated driving measures of lane position, speed, crash occurrence and reaction times [31,33,44]. On simulated driving tasks PERCLOS has been shown to predict lateral position (r = .61), but not speed, braking reaction time or crashes [32]. In addition, JDS has fair ability (AUC = .76) for predicting off-road events following extended wakefulness [44]. These findings suggest that eye blink parameters have the potential to detect driving performance impairment secondary to drowsiness.

On road driving

During on road closed track driving video measured blink rate and blink duration were significant but poor predictors of lane departure (AUC = .66 and .63 respectively) [34]. Liang [45] utilised data from Lee [37] and demonstrated that the addition of infrared oculography parameters of eye closure, eyelid closing/reopening speed and the JDS, significantly improved a lane crossing prediction model changing the detection ability from fair (AUC = .72 – with subjects factors only) to between good to excellent (AUC = .84-.90). A similar improvement was observed when eye blink parameters were added to an EEG micro-sleep prediction model (AUC = .81 – with subjects factors only, to AUC = .84-.94 when eye blink parameters were added) but the difference did not reach significance [45].

During real on road driving, EOG blink duration has been shown to predict lateral lane position (slope = −0.060 and standard error = 0.008) [16] as well as lane departures [22]. A study that assessed regular commuting in shift workers across two weeks found that eye blink parameters recorded via infrared oculography had the highest adjusted odd-ratios for self-reported sleep events (blink duration OR = 5.35) and inattention events (JDS <4.5 vs ≥ 4.5 OR = 4.58) [29]. For self-reported hazard and violation events, KSS and time awake were significant predictors but eye blink parameters were not. This suggests that eye blink parameters may be better at identifying driving impairments specific to sleep, rather than driving impairment in general.

Summary

Eye blink parameters moderately to strongly correlated with conventional drowsiness measures in most publications. Table 3 summarises the findings of studies that assessed the ability of eye blink parameters to predict conventional drowsiness measures. The parameters of blink duration, percentage of eye closure and composite JDS were most thoroughly studied and were shown to consistently relate to and predict neurobehavioral task performance and subjective sleepiness with an AUC accuracy that was mostly fair to good. JDS and percentage of eye closure also showed promise for predicting simulated driving but were each assessed in a single study only. Blink duration was evaluated in several on road driving studies and predicted driving impairment in a majority, suggesting it is a promising in-field assessment tool. For eye blink frequency and eyelid closing/opening speed, a few studies showed potential predictive ability, but further validation work is required before they could be considered a reliable drowsiness measure. A limitation of the studies listed in Table 3, is that for those studies that utilised AUC to assess detection accuracy (as indicated by * symbols), all but one were conducted in controlled laboratory environments. Therefore further work is required to determine whether detection accuracy is similar during uncontrolled naturalistic driving or operational settings where other extraneous factors are present. Additionally, variation in detection accuracy within Table 3 may be attributed to acquisition technology. Therefore further work should assess different acquisition technologies simultaneously to determine whether they result in different accuracies and if so, which is best for drowsiness detection.

Section 3 – How useful are eye blink parameters for detecting state drowsiness in obstructive sleep apnoea patients?

OSA is a common sleep-breathing disorder that affects ~10% of adults [53]. OSA is characterised by repeated upper airway collapse during sleep. Consequences include sleep fragmentation, intermittent hypoxia, excessive daytime sleepiness and neurocognitive impairment [54]. OSA is associated with a two to three-fold increase in motor vehicle accident risk [55], but not all OSA patients are affected by sleepiness [56] and there is no simple objective method of identifying affected individuals. The maintenance of wakefulness test (MWT) is an objective sleepiness measure [57] recommended for fitness to drive assessment [58], but the task does not replicate the driving scenario. Limited studies have demonstrated that MWT has a weak to moderate relationship with driving impairment [59–61]. Because of cost MWT is typically restricted to severe patients or those in high risk occupations. Measuring eye blink parameters presents an alternative option for fitness to drive assessment in OSA. An advantage of eye blink based drowsiness monitoring is the ability to continuously assess drowsiness during regular driving over days, weeks or months, enabling assessment during increased risk scenarios such as extended or evening driving. An additional benefit is the capability for automated analysis, which may reduce cost relative to the MWT, which requires specialised manual analysis. However, to date, only a few studies have evaluated eye blink measures of drowsiness in OSA and their ability to predict real world crash risk has not been assessed.

One study demonstrated that eye blink parameters may be as useful as MWT for detecting sleepiness and treatment response in OSA patients. Relative to healthy controls, OSA patients had longer

Table 3
Summary table of studies that have assessed the ability of eye blink parameters to predict existing drowsiness measures of subjective sleepiness, neurobehavioral performance, EEG, simulated driving and on road driving. X/X denotes the number of studies in which eye blink parameters successfully predicted existing drowsiness measures.

	Subjective Sleepiness	PVT and OSLER	EEG	Simulated Driving	On road Driving	Total
Blink Duration	2/2 Anderson C et al., 2013 [3] *** Sandberg D et al., 2011 [16] S	4/4 Abe T et al., 2011 [28] ** Anderson C et al., 2013 [3] ** Ftouni S et al., 2013 [39] *** Wilkinson VE et al., 2013 [41] ****	0/0	0/0	3/4 Ftouni S et al., 2013 [29] S Hallvig D et al., 2014 [22] S Sandberg D et al., 2011 [16] S Shiferaw BA et al., 2018 [34] **	**9/10**
Percentage of Eye Closure	1/2 Anderson C et al., 2013 [3] *** Jackson ML et al., 2016 [32] NS	6/6 Abe T et al., 2011 [28] **** Anderson C et al., 2013 [3] *** Ftouni S et al., 2013 [39] ** Jackson ML et al., 2016 [31] **** Jackson ML et al., 2016 [32] S Wilkinson VE et al., 2013 [41] **	0/0	1/1 Jackson ML et al., 2016 [32] S	1/1 Ftouni S et al., 2013 [29] S	**9/10**
Eye blink Frequency	0/0	1/1 Abe T et al., 2011 [28] ***	0/0	0/0	1/1 Shiferaw BA et al., 2018 [34] **	**2/2**
Eyelid closing/reopening speed	1/1 Anderson C et al., 2013 [3] **	3/3 Anderson C et al., 2013 [3] ** Ftouni S et al., 2013 [39] **** Wilkinson VE et al., 2013 [41] ***	0/0	0/0	0/0	**4/4**
Composite JDS	1/1 Anderson C et al., 2013 [3] ****	3/3 Anderson C et al., 2013 [3] *** Ftouni S et al., 2013 [39] *** Wilkinson VE et al., 2013 [41] ***	0/0	1/1 Johns MW et al., 2008 [44] ***	1/1 Ftouni S et al., 2013 [29] S	**6/6**
Total	**5/6**	**17/17**	**0/0**	**2/2**	**6/7**	

Note only studies that reported significance values or area under the curve (AUC) values are reported. For studies that reported AUC ***** denotes excellent accuracy .99-.90, **** good accuracy .89-.80, *** fair accuracy .79-.70, ** poor accuracy .69-.60 and * fail .59 or less. When studies measured multiple parameters for the same eye blink category the best AUC was indicated in the table. For studies that did not report AUC, S denotes a significant predictor and NS a non-significant predictor. PVT – Psychomotor vigilance test, OSLER – Oxford sleepiness resistance test and EEG-electroencephalogram.

eye blink durations measured via video during real on road driving and shorter sleep latencies on the MWT indicating greater sleepiness [36]. However, following nine weeks of continuous positive airway treatment (CPAP), blink duration and MWT latencies were no longer different from controls. There is also indication that eye blink parameters may distinguish between OSA patients with and without sleepiness [42]. For OSA patients who reported excessive daytime sleepiness, a single night of CPAP reduced infrared oculography blink duration by 13%, eyelid reopening time by 17% and increased blink frequency by 29%. In contrast, for OSA patients who did no report excessive daytime sleepiness there was no improvement in eye blink parameters following treatment. Another study suggested that eye blink parameters could predict driving impairment in OSA, as EOG long closures (>2 s) had an OR of 7.2 for detecting at least one crash event in OSA patients assessed on a driving simulator following restricted sleep (4 h TIB) [62]. More recently it was demonstrated that infrared oculography eye blink parameters measured during simple laboratory tasks could distinguish between OSA patients and healthy controls [43]. −AVR was consistently greater in OSA patients regardless of the assessment tasks which comprised a driving simulation (high complexity), PVT (moderate complexity) and OSLER (minimal complexity). Blink duration was a useful discriminator during the PVT and OSLER and %LEC only during the OSLER. This highlights the potential for these measures to be utilised in the laboratory with -AVR likely to be sensitive irrespective of task complexity. However, further work needs to be done, to determine whether these measures actually link to sleepiness related on road driving impairment in this patient population.

Summary

Limited studies have demonstrated that eye blink measures are able to distinguish between OSA patients and healthy controls, identify OSA patients affected by drowsiness and evaluate OSA treatment response. Fitness to drive assessment in OSA is challenging given current recommended laboratory assessments (MWT) are expensive and not strongly related to crash risk. Eye blink parameters measured while driving provide the opportunity to assess drowsiness in field. Propriety devices that are suitable for extended monitoring during driving and provide automated analysis could be used for this purpose. However, whether eye blink measures provide a better measure of drowsiness than the MWT remains to be assessed. Given device cut-off scores have been established in relation to sleep deprived healthy individuals [47], cut-off scores related to driving impairment in an OSA population will need to be established. However, compliance may be a potential caveat of these devices, as patients may choose not to drive if they are drowsy and know they are being monitored.

Discussion

This review demonstrated that irrespective of whether drowsiness impairment was due to extended wakefulness or reduced circadian alertness, eye blink parameters consistently changed in a predictable direction. These results were similar across both laboratory and field settings as well as different assessment tasks irrespective of degree of engagement and complexity. Eye blink parameters were shown to be associated with, and predictive of conventional drowsiness measures. These findings support the use of eye blink parameters for drowsiness monitoring in operational settings such as the transport and mining industry, where they provide an advantage over conventional drowsiness measures. In these sectors, these technologies could also be used to evaluate the impact of other interventions, such as scheduling changes. Another potential application of eye blink parameters is clinical drowsiness assessment during regular driving in OSA. However, further research is required to determine if this would improve detection capability beyond the currently recommended fitness to drive measures.

Blink duration and percentage of eye closure metrics were the most frequently assessed eye blink parameters and the most consistent for drowsiness detection. These parameters predicted conventional drowsiness outcomes with an accuracy that typically ranged from fair to good (see Table 3). Blink duration is recommended for operational drowsiness assessment because it was extensively evaluated across both laboratory and field settings and conditions of extended wakefulness and low circadian alertness. Blink rate was the least reliable metric and is not recommended for operational drowsiness assessment. Eyelid closing/reopening speed and composite measures showed promise but require further evaluation before being considered useful indicators of drowsiness.

The few studies that assessed OSA, showed that eye blink parameters distinguished between individuals with and without OSA [36,43], OSA patients with and without excessive daytime sleepiness [42] and OSA patients with and without treatment [36]. Therefore, eye blink parameters have the potential to be used as a clinical tool to identify OSA patients at risk of drowsiness impairment and to assess their treatment response. Existing fitness to drive assessments are reliant on self-report or involve complex laboratory tasks that bear little resemblance to actual driving behaviour and have limited relationship to crash risk [61]. The advantage of propriety eye blink drowsiness monitoring devices is that they can be used during regular on road driving, over an extended time period and have automated analysis with easy to interpret output. And, while they would not be required in the case where a patient self-reports drowsiness and related near-accidents while driving, they may assist clinicians in cases where OSA is moderate to severe, but the patient does not report drowsiness symptoms and objective assessment is warranted to determine fitness to drive. However, before eye blink parameters can be utilised as a drowsiness assessment tool in OSA, further work is required to determine whether they are capable of detecting real world driving impairment relating to drowsiness, and how they compare to the existing clinical drowsiness assessment tools.

While eye blink measures show great promise for drowsiness assessment they do have some limitations which include the inability to accurately monitor drowsiness when the user is moving, the need for the technology to be worn or be in a fixed position, and the potential requirement for individual calibration. Therefore, improvements in technology are required to enable accurate and reliable drowsiness monitoring across a range of different user scenarios, as well as to maximise user compliance and acceptability.

Despite their limitations eye blink parameters should be utilised when they can provide a practical advantage over conventional drowsiness metrics. For instance, eye blink drowsiness monitoring is a suitable tool to assist in fatigue management in the transport industry where drowsiness risk is high due to long hours, shiftwork and the repetitive work nature. In this scenario, using a subjective measure may not be a reliable indicator of drowsiness and use of a neurobehavioral assessment such as the PVT would be disruptive to regular duties. In contrast, using eye blink monitoring devices that are worn or installed in cabin could provide a relatively non-invasive, objective continuous measure that enables real-time feedback on drowsiness state. These devices are already being trialled by some companies within the transport industry [46], with preliminary evidence suggesting that device feedback does indeed modify alertness levels and improve driver performance [46,63].

However, it unknown yet as to whether the improvements are long lasting. Additionally, it is not clear whether improvements to alertness are a result of the device warnings themselves or via indirect behavioural changes as a result of being monitored (e.g., increasing sleep or using caffeine, etc.). However, regardless of the mechanism, these preliminary findings indicate a positive impact of these devices on alertness levels.

In summary, eye blink measures of drowsiness show promise as a tool that can be used for continuous drowsiness state assessment in both operational and clinical settings when they provide an advantage over existing measures. However further validation work in larger samples is required, particularly to understand individual variability in these parameters which has only received minimal attention to date [64,65] and how they vary in relation to standard population demographics such age and gender. Additionally, given the vast array of technologies (video, infrared and EOG), future work needs to directly compare these measures to determine which of these are most effective and practical for use in respective operational and clinical environments.

Practice Points

1. Eye blink parameters consistently change in a predictable direction in association with drowsiness induced by conditions of extended wakefulness and low circadian alertness.
2. Eye blink parameters moderately to strongly correlate with performance on conventional state measures of drowsiness and are capable of predicting outcomes on these measures with fair to good accuracy.
3. Eye blink parameters distinguish between individuals with and without sleep apnoea, sleep apnoea patients with and without excessive daytime sleepiness as well as treated and untreated sleep apnoea patients.

Research Agenda

1. To further validate eye blink parameters as a drowsiness assessment tool, studies need to assess larger sample sizes and an older age range. In addition, interindividual differences in these parameters need to be better understood.
2. Eye blink parameters as a drowsiness indicator should be further assessed in operational settings and the influence of feedback from such measures on behaviour and alertness levels should be examined.
3. Eye blink parameters should be investigated as a potential clinical tool to identify sleep apnoea patients at risk of drowsiness related driving impairment.

Conflicts of interest

Jennifer M. Cori, Clare Anderson, Shamsi Shekari Soleimanloo and Mark E. Howard have received research support from Seeing Machines Ltd, Optalert Ltd and the Cooperative Research Centre for Alertness Safety and Productivity.

References

[1] Corsi-Cabrera M, Arce C, Ramos J, Lorenzo I, Guevara MA. Time course of reaction time and EEG while performing a vigilance task during total sleep deprivation. Sleep 1996;19:563–9.
[2] Anund A, Kecklund G, Peters B, Forsman A, Lowden A, Akerstedt T. Driver impairment at night and its relation to physiological sleepiness. Scand J Work Environ Health 2008;34:142–50.
*[3] Anderson C, Chang A-M, Sullivan JP, Ronda JM, Czeisler CA. Assessment of drowsiness based on ocular parameters detected by infrared reflectance oculography. J Clin Sleep Med 2013;9:907–20.
[4] Dingus TA, Guo F, Lee S, Antin JF, Perez M, Buchanan-king M, et al. Driver crash risk factors and prevalence evaluation using naturalistic driving data. Proc Natl Acad Sci Unit States Am 2016;113:2636–41.
[5] Horne JA, Reyner LA. Sleep related vehicle accidents. BMJ 1995;310:565–7.
[6] Rajaratnam SMW, Barger LK, Lockley SW, Shea SA, Wang W, Landrigan CP, et al. Sleep disorders, health and safety in police officers. J Am Med Assoc 2011;306:2567–78.
[7] Åkerstedt T, Gillberg M. Subjective and objective sleepiness in the active individual. Int J Neurosci 1990;52:29–37.
[8] Horne JA, Burley CV. We know when we are sleepy: subjective versus objective measurements of moderate sleepiness in healthy adults. Biol Psychol 2010;83:266–8.
[9] Anderson C, Ftouni S, Ronda JM, Rajaratnam SMW, Czeisler CA, Lockley SW. Self-reported drowsiness and safety outcomes while driving after an extended duration work shift in trainee physicians. Sleep 2018;41(2):1–11.
[10] Howard ME, Jackson ML, Berlowitz D, O'Donoghue F, Swann P, Westlake J, et al. Specific sleepiness symptoms are indicators of performance impairment during sleep deprivation. Accid Anal Prev 2014;62:1–8.
[11] Van Dongen HPA, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 2003;26:117–26.
[12] Dawson D, Searle AK, Paterson JL. Look before you (s)leep: evaluating the use of fatigue detection technologies within a fatigue risk management system for the road transport industry. Sleep Med Rev 2014;18:141–52.
[13] Barbato G, Ficca G, Beatrice M, Casiello M, Muscettola G, Rinaldi F. Effects of sleep-deprivation on spontaneous eye blink rate and alpha-eeg power. Biol Psychiatry 1995;38:340–1.
[14] Barbato G, De Padova V, Paolillo AR, Arpaia L, Russo E, Ficca G. Increased spontaneous eye blink rate following prolonged wakefulness. Physiol Behav 2007;90:151–4.
[15] Anund A, Kecklund G, Kircher A, Tapani A, Akerstedt T. The effects of driving situation on sleepiness indicators after sleep loss: a driving simulator study. Ind Health 2009;47:393–401.
*[16] Sandberg D, Anund A, Fors C, Kecklund G, Karlsson JG, Wahde M, et al. The characteristics of sleepiness during real driving at night–a study of driving performance, physiology and subjective experience. Sleep 2011;34:1317–25.
[17] Åkerstedt T, Hallvig D, Anund A, Fors C, Schwarz J, Kecklund G. Having to stop driving at night because of dangerous sleepiness - awareness, physiology and behaviour. J Sleep Res 2013;22:380–8.
[18] Anund A, Fors C, Hallvig D, Åkerstedt T, Kecklund G. Observer rated sleepiness and real road driving: an explorative study. PLoS One 2013;8:1–18.
[19] Ahlström C, Anund A, Fors C, Åkerstedt T. The effect of daylight versus darkness on driver sleepiness: a driving simulator study. J Sleep Res 2017;2:1–9.
[20] Anund A, Ahlstrom C, Fors C, Akerstedt T. Are professional drivers less sleepy than non-professional drivers? Scand J Work Environ Health 2018;44:88–95.
[21] Ahlström C, Anund A, Fors C, Åkerstedt T. Effects of the road environment on the development of driver sleepiness in young male drivers. Accid Anal Prev 2018;112:127–34.
*[22] Hallvig D, Anund A, Fors C, Kecklund G, Åkerstedt T. Real driving at night - predicting lane departures from physiological and subjective sleepiness. Biol Psychol 2014;101:18–23.
[23] Cajochen C, Khalsa SB, Wyatt JK, Czeisler CA, Dijk DJ. EEG and ocular correlates of circadian melatonin phase and human performance decrements during sleep loss. Am J Physiol 1999;277:R640–9.
[24] Barbato G, Ficca G, Muscettola G, Fichele M, Beatrice M, Rinaldi F. Diurnal variation in spontaneous eye-blink rate. Psychiatr Res 2000;93:145–51.
[25] De Padova V, Barbato G, Conte F, Ficca G. Diurnal variation of spontaneous eye blink rate in the elderly and its relationships with sleepiness and arousal. Neurosci Lett 2009;463:40–3.
[26] De Gennaro L, Devoto A, Lucidi F, Violani C. Oculomotor changes are associated to daytime sleepiness in the multiple sleep latency test. J Sleep Res 2005;14:107–12.
[27] Åkerstedt T, Ingre M, Kecklund G, Anund A, Sandberg D, Wahde M, et al. Reaction of sleepiness indicators to partial sleep deprivation, time of day and time on task in a driving simulator - the DROWSI project. J Sleep Res 2010;19:298–309.

* The most important references are denoted by an asterisk.

[28] Abe T, Nonomura T, Komada Y, Asaoka S, Sasai T, Ueno A, et al. Detecting deteriorated vigilance using percentage of eyelid closure time during behavioral maintenance of wakefulness tests. Int J Psychophysiol 2011;82:269–74.
*[29] Ftouni S, Sletten TL, Howard M, Anderson C, Lenné MG, Lockley SW, et al. Objective and subjective measures of sleepiness, and their associations with on-road driving events in shift workers. J Sleep Res 2013;22:58–69.
[30] Åkerstedt T, Peters B, Anund A, Kecklund G. Impaired alertness and performance driving home from the night shift: a driving simulator study. J Sleep Res 2005;14:17–20.
[31] Jackson ML, Kennedy GA, Clarke C, Gullo M, Swann P, Downey LA, et al. The utility of automated measures of ocular metrics for detecting driver drowsiness during extended wakefulness. Accid Anal Prev 2016;87:127–33.
[32] Jackson ML, Raj S, Croft RJ, Hayley AC, Downey LA, Kennedy GA, et al. Slow eyelid closure as a measure of driver drowsiness and its relationship to performance. Traffic Inj Prev 2016;17:251–7.
[33] Alvaro PK, Jackson ML, Berlowitz DJ, Swann P, Howard ME. Prolonged eyelid closure episodes during sleep deprivation in professional drivers. J Clin Sleep Med 2016;12:1099–103.
*[34] Shiferaw BA, Downey LA, Westlake J, Stevens B, Rajaratnam SMW, Berlowitz DJ, et al. Stationary gaze entropy predicts lane departure events in sleep-deprived drivers. Sci Rep 2018;8:1–10.
[35] Slama H, Chylinski DO, Deliens G, Leproult R, Schmitz R, Peigneux P. Sleep deprivation triggers cognitive control impairments in task-goal switching. Sleep 2018;41:1–12.
*[36] Häkkänen H, Summala H, Partinen M, Tiihonen M, Silvo J. Blink duration as an indicator of driver sleepiness in professional bus drivers. Sleep 1999;22:798–802.
*[37] Lee ML, Howard ME, Horrey WJ, Liang Y, Anderson C, Shreeve MS, et al. High risk of near-crash driving events following night-shift work. Proc Natl Acad Sci Unit States Am 2016;113:176–81.
[38] Caffier PP, Erdmann U, Ullsperger P. Experimental evaluation of eye-blink parameters as a drowsiness measure. Eur J Appl Physiol 2003;89:319–25.
*[39] Ftouni S, Rahman SA, Crowley KE, Anderson C, Rajaratnam SMW, Lockley SW. Temporal dynamics of ocular indicators of sleepiness across sleep restriction. J Biol Rhythm 2013;28:412–24.
*[40] Ftouni S, Sletten TL, Nicholas CL, Kennaway DJ, Lockley SW, Rajaratnam SMW. Ocular measures of sleepiness are increased in night shift workers undergoing a simulated night shift near the peak time of the 6-sulfatoxymelatonin rhythm. J Clin Sleep Med 2015;11:1131–1141A.
[41] Wilkinson VE, Jackson ML, Westlake J, Stevens B, Barnes M, Swann P, et al. The accuracy of eyelid movement parameters for drowsiness detection. J Clin Sleep Med 2013;9:1315–24.
*[42] Caffier PP, Erdmann U, Ullsperger P. The spontaneous eye-blink as sleepiness indicator in patients with obstructive sleep apnoea syndrome-a pilot study. Sleep Med 2005;6:155–62.
[43] Cori JM, Jackson ML, Barnes M, Westlake J, Emerson P, Lee J, et al. The differential effects of regular shift work and obstructive sleep apnea on sleepiness, mood and neurocognitive function. J Clin Sleep Med 2018;14:941–51.
[44] Johns MW, Chapman R, Crowley K, Tucker A. A new method for assessing the risks of drowsiness while driving. Somnologie 2008;12:66–74.
[45] Liang Y, Horrey WJ, Howard ME, Lee ML, Anderson C, Shreeve MS, et al. Prediction of drowsiness events in night shift workers during morning driving. Accid Anal Prev 2017. https://doi.org/10.1016/j.aap.2017.11.004.
[46] Fitzharris M, Liu S, Stephens AN, Lenné MG. The relative importance of real-time in-cab and external feedback in managing fatigue in real-world commercial transport operations. Traffic Inj Prev 2017;18:S71–8.
[47] Johns MW, Tucker A, Chapman R, Crowley K, Michael N. Monitoring eye and eyelid movements by infrared reflectance oculography to measure drowsiness in drivers. Somnologie 2007;11:234–42.
[48] Philip P, Sagaspe P, Taillard J, Valtat C, Moore N, Akerstedt T, et al. Fatigue, sleepiness, and performance in simulated versus real driving conditions. Sleep 2005;28:1511–6.
[49] Ong JL, Asplund CL, Chia TTY, Chee MWL. Now you hear me, now you don't: eyelid closures as an indicator of auditory task disengagement. Sleep 2013;36:1867–74.
[50] François C, Hoyoux T, Langohr T, Wertz J, Verly JG. Tests of a new drowsiness characterization and monitoring system based on ocular parameters. Int J Environ Res Public Health 2016;13:1–10.
[51] Bartolucci AA, Singh KP, Sejong B. Chapter 3: method validation. Introd to stat anal lab data. Illustrated. John Wiley & Sons, Ltd.; 2015. p. 43–76.
[52] Bennett LS, Stradling JR, Davies RJO. A behavioural test to assess daytime sleepiness in obstructive sleep apnoea. J Sleep Res 1997;6:142–5.
[53] Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013;177:1006–14.
[54] Patil SP, Schneider H, Schwartz AR, Smith PL. Adult obstructive sleep apnea: pathophysiology and diagnosis. Chest 2007;132:325–37.
[55] Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. J Clin sleep Med 2009;5:573–81.
[56] Vakulin A, Catcheside PG, Baulk SD, Antic NA, Banks S, Dorrian J, et al. Individual variability and predictors of driving simulator impairment in patients with obstructive sleep apnea. J Clin Sleep Med 2014;10:647–55.
[57] Littner M, Kushida C, Wise M, Davila D, Morgenthaler T, Lee-Chiong T, et al. Practice parameters for clinical use of the multiple sleep latecy test and the maintenance of wakefulness test. Sleep 2005;28:113–21.
[58] Austroads and National Transport Commission Australia. Assessing fitness to drive for commercial and private vehicle drivers. Medical Standards for Licensing and Clinical Management Guidelines. 2016.
[59] Philip P, Sagaspe P, Taillard J, Chaumet G, Bayon V, Coste O, et al. Maintenance of wakefulness test, obstructive sleep apnea syndrome, and driving risk. Ann Neurol 2008;64:410–6.
[60] Philip P, Chaufton C, Taillard J, Sagaspe P, Léger D, Raimondi M, et al. Maintenance of Wakefulness Test scores and driving performance in sleep disorder patients and controls. Int J Psychophysiol 2013;89:195–202.
[61] Kingshott RN, Cowan JO, Jones DR, Flannery EM, Smith AD, Herbison GP, et al. The role of sleep-disordered breathing, daytime sleepiness, and impaired performance in motor vehicle crashes — a case control study. Sleep Breath 2004;8:61–72.
[62] Vakulin A, Baulk SD, Catcheside PG, Antic NA, Heuvel CJ Van Den, Dorrian J, et al. Effects of alcohol and sleep restriction on simulated driving performance in untreated patients with obstructive sleep apnea. Ann Intern Med 2009;151:447–55.
[63] Aidman E, Chadunow C, Johnson K, Reece J. Real-time driver drowsiness feedback improves driver alertness and self-reported driving performance. Accid Anal Prev 2015;81:8–13.
[64] Chua EC-P, Yeo S-C, Lee IT-G, Tan L-C, Lau P, Tan SS, et al. Individual differences in physiologic measures are stable across repeated exposures to total sleep deprivation. Phys Rep 2014;2:1–16.
[65] Ingre M, Åkerstedt T, Peters B, Anund A, Kecklund G. Subjective sleepiness, simulated driving performance and blink duration: examining individual differences. J Sleep Res 2006;15:47–53.