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Now You Hear Me, Now You Don't: Eyelid Closures as an Indicator of Auditory Task Disengagement

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Study Objectives: Eyelid closures in fatigued individuals signify task disengagement in attention-demanding visual tasks. Here, we studied how varying degrees of eyelid closure predict responses to auditory stimuli depending on whether a participant is well rested or sleep deprived. We also examined time-on-task effects and how more and less vulnerable individuals differed in frequency of eye closures and lapses.
Design: Six repetitions of an auditory vigilance task were performed in each of two sessions: rested wakefulness (RW) and total sleep deprivation (TSD) (order counterbalanced).
Setting: Sleep laboratory.
Participants: Nineteen healthy young adults (mean age: 22 ± 2.8 y; 11 males).
Intervention: Approximately 24 h of TSD.
Measurements and Results: Eyelid closure was rated on a 9-point scale (1 = fully closed to 9 = fully opened) using video segments time-locked to the auditory event. Eyes-open trials predominated during RW, but different degrees of eye closure were uniformly distributed during TSD. The frequency of lapses (response time > 800 ms or nonresponses) to auditory stimuli increased dramatically with greater degrees of eye closure, but the association was strong only during TSD. There were significant within-run time-on-task effects on eye closure and auditory lapses that were exacerbated by TSD. Participants who had more auditory lapses during TSD (more vulnerable) had greater variability in their eyelid closures.
Conclusions: Eyelid closures are a strong predictor of auditory task disengagement in the sleep-deprived state but are less relevant during rested wakefulness. Individuals relatively more impaired in this auditory vigilance task during total sleep deprivation display oculomotor evidence for greater state instability.

Keywords: Auditory attention, eye closure, sleep deprivation, sustained attention, time on-task
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INTRODUCTION

Failures in vigilance or sustained attention cause the most commonly observed behavioral changes in sleep-deprived persons.[1] These failures are problematic because timely responses to visual stimuli may be critical in transport and security settings. A triad of slower responses, increased nonresponses, and increased false alarms are found in tasks requiring speeded responses to temporally unpredictable targets, such as the Psychomotor Vigilance Task (PVT).[2] While dependably indicative of failures in attention as well as attempts at compensation,[3] such behavioral assays are intrusive and interfere with concurrent performance of other tasks.[4]

Physiological monitoring of oculomotor variables, including blink duration, delay in lid reopening, blink velocity, slow eye movements, and/or percentage eyelid closure over 1 min (PERCLOS) provide complementary measures of vigilance that are nonintrusive.[5-11] Moment-to-moment fluctuations in such measures are associated with behavioral changes, thus providing a window into the processes underlying reduced responsiveness to the external environment. Such correlations have been studied with visual stimuli,[12,13] but less is known about the relationship between eye closures and performance when stimuli are presented in other sensory modalities. As eyelids act as a physical barrier to visual stimuli, it is trivial to expect that eye closure will impair visual target detection. What about auditory targets?

On the one hand, perception of auditory stimuli should not be negatively affected by eye closure alone. We can 'close our eyes' to visual stimuli but there is no analogous process for shutting out auditory stimuli. Vehicular safety systems take advantage of this difference by using other sensory modalities to deliver information and warnings. For example, new systems seek to improve driver performance by presenting congruent multisensory stimuli,[10,11] and aircraft landing systems use auditory warning signals. Neural evidence also supports these strategies: voluntary eye closure is associated with increased activation in sensory cortices, including auditory cortex.[14]

On the other hand, most eye closures originating from fatigue and sleep deprivation are involuntary, a consequence of diminished wake drive.[10,15,16] During sleep itself, stimulus-evoked responses in auditory and visual cortex are reduced,[17] and auditory awakening thresholds are increased.[18] These altered thresholds could also reflect diminished higher cortical processing of sensory inputs, unless the incoming stimuli are particularly salient.[19] Reduced auditory processing may be present in the sleep-deprived state as well, with eye closures indexing the severity of the impairment. Consequently, presenting auditory stimuli may not completely alleviate the problems of eye closure during sleep deprivation.

Eye closure is not fully predictive of behavioral deficits when visual tasks are performed. Long reaction times

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and nonresponses (together termed lapses) can occur when the eyes are either fully or partially opened.[12] However, the long-duration, eyes-closed lapses that are thought to denote microsleeps are potentially more important than these shorter-duration, eyes-open lapses from a safety viewpoint.[12,13,20] Both types of lapses increase with sleep deprivation, especially with the continued performance of an attention-demanding task.[21] These time-on-task effects have been primarily reported from visual tasks and are much less well characterized for other modalities.

The current study addresses some of these gaps in our knowledge by evaluating whether the degree of eyelid closure is related to responses to auditory stimuli during sleep deprivation or rested wakefulness. We also examine how sleep deprivation interacts with time-on-task to modulate eye closure and behavioral performance. Finally, we evaluate how an individual's vulnerability to TSD relates to the observed range of partial eye closures.

MATERIALS AND METHODS

Participants

Twenty-nine healthy young adults from the National University of Singapore were selected from respondents to a web-based questionnaire who: (1) were between 18-35 y of age, (2) were non-smokers, (3) had no history of psychiatric, neurological, or sleep disorders, (4) consumed no more than two caffeinated drinks per day, (5) had good habitual sleep between 6.5-9 h daily (i.e., sleeping before 00:30 and getting up before 09:00), and (6) were not of an extreme chronotype as assessed on a reduced version of the Horne-Östberg Morningness-Eveningness questionnaire.[22] All participants provided informed consent in compliance with a protocol approved by the National University of Singapore Institutional Review Board, and were paid for their involvement.

From this initial pool, 24 subjects fully complied with study protocols and completed both the rested wakefulness (RW) and TSD sessions of the study. One subject was removed from further analyses because of frequent nonresponses (22%) recorded in the RW session. An additional 4 participants had to be excluded due to eye-tracker equipment issues. The remaining 19 participants (11 male), aged 22 ± 2.8 y (mean ± standard deviation), were included in the final analyses.

Laboratory Protocol

Participants made three visits to the laboratory. On their first visit, they were briefed on the study protocol and tasks to be undertaken. They also collected a wrist actigraph (Actiwatch 2, Respironics, Inc., Murrysville, PA), which they were instructed to wear at all times for the duration of the experiment. The device monitored compliance with the required 6.5-9 h sleep-wake schedules in each week preceding a test session.

Approximately 1 w after the briefing session, participants returned to the laboratory for the first of two in-scanner sessions (functional magnetic resonance imaging [fMRI] findings are not reported here). The order of session type, TSD or RW, was counterbalanced across participants. The second scanner session was scheduled at least 1 w after the first to provide adequate recovery from the effects of sleep loss in the event that the TSD session preceded the RW session.[23] Participants refrained from consuming alcohol and caffeinated beverages 24 h prior to the start of either session.

For the RW session, participants reported to the laboratory at 20:30 the night before their scheduled scan session and underwent overnight polysomnography (PSG) to ensure that they had approximately 8 h of sleep prior to the RW session. Participants went to bed no later than 23:00 and were awakened at 07:00 the following morning. Total sleep time (TST) for the night prior to the RW session was 7.9 ± 0.5 h (mean ± standard deviation). In order to mitigate any effects of sleep inertia, participants were given 1 h to wash up and have a light snack. Prior to the scan, participants also completed a 10-min visual PVT on a handheld device,[2] the 9-point Karolinska Sleepiness Scale (KSS)[24] probing subjective sleepiness, and questionnaires assessing mood and personality for a separate study.

For the TSD session, participants reported to the laboratory at 19:00 and were kept awake overnight under the constant supervision of a research assistant. During this period, they were allowed to engage in light recreational activities such as reading or watching films. During the first hour of their TSD session, participants also completed the Epworth Sleepiness Scale (ESS).[25] They performed a total of ten 10-min visual PVTs on the hour between 20:00 and 05:00 and a single KSS assessment at 05:20. The session times were chosen to be representative of a typical work day start time (RW session) and the time when vigilance hits a nadir following a night of sleep deprivation (TSD session).[26]

Experimental Task

Participants performed the auditory vigilance task twice, once after a normal night of sleep at approximately 08:00 and once after 22-24 h of total sleep deprivation at approximately 06:00. In this task, they heard an auditory tone resembling a low-frequency beep (see auditory tone sample included in supplemental material) and responded as quickly as possible by pressing a response grip with the right index finger (Nordic Neurolab, Bergen, Norway). So that a range of eye closure and response behavior could be observed, these test tones were of moderate intensity and not affectively or semantically meaningful (e.g., persons' name or car horn), as such stimuli have been known to elicit superior performance[27] as well as greater higher cortical engagement.[19] The tones were 200 ms in duration (10-ms onset and offset ramps) and were delivered binaurally via pneumatic headphones. To eliminate foreperiod (FP) effects that can modulate response times (RTs) based on trial history,[28] stimulus onset intervals (SOA) ranging from 4-12 sec (mean = 6 sec) were randomly sampled from an exponential distribution (decay constant, $\tau = 2.03$) so that trials with shorter FPs would occur more frequently than those with longer ones. A total of 600 such tones were presented across six 10-min runs, separated by 1-min breaks.

To ensure that participants could hear the target over scanner noise, a 1-up-1-down staircase thresholding procedure was performed during a scan. This defined the 50% detection threshold volume for each participant. So that the target tone could be clearly heard during the main experiment, stimuli were adjusted to have 4 times the amplitude of the threshold

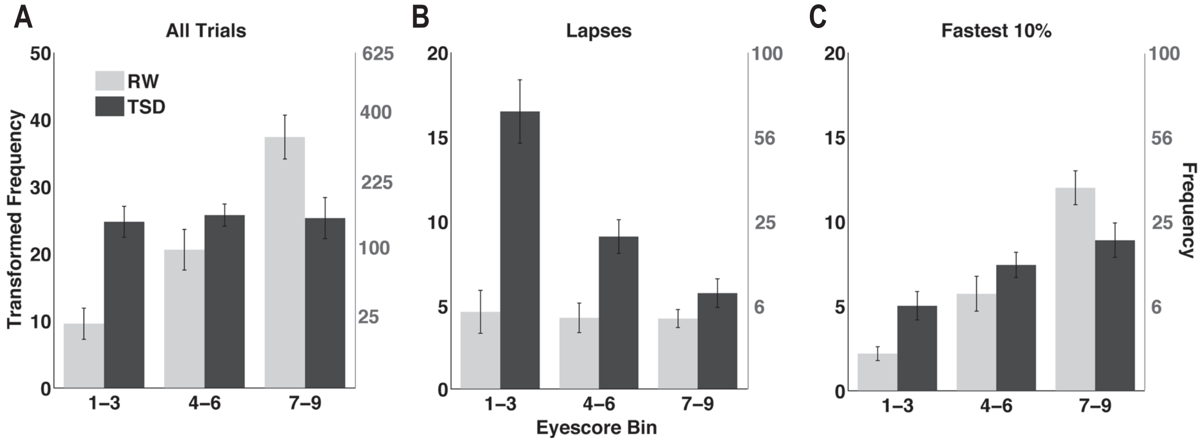

Figure 1—Frequency of ES occurrence (right axis) and transformed frequency (left axis) for **(A)** all trials, **(B)** lapses (RT > 800 ms) and **(C)** fastest 10% in the RW (light gray bars) and TSD (dark gray bars) states collapsed into 3 eyescore bins. Transformations were performed for ANOVA analyses using $\sqrt{n}+\sqrt{n+1}$,[12,29] where n = number of trials in each eyescore bin. Error bars represent standard error of the mean. ANOVA, analysis of variance; ES, eyescore, RT, response time; RW, rested wakefulness; TSD, total sleep deprivation

signal. These tones were softer than the wake-up calls (see the following paragraphs) at 10 times detection threshold.

As the auditory vigilance task was carried out in a darkened room while the patient was lying supine, it could be performed with the eyes closed. It was therefore imperative to ensure that subjects made a reasonable effort to keep their eyes open while listening for the auditory target stimulus/tone. We used two methods to ensure this: we had participants keep a look out for a clearly visible yet rare visual target and we incentivized them to do so. Participants earned $1.00 for each color change detected in the central fixation dot (gray to green). These transient changes (500 ms) occurred very rarely, from 1-3 times per 10-min run, and were unlikely to affect auditory detection. The same minimal incentives and secondary tasks were applied in both rested and sleep-deprived states.

Visual stimuli were presented using a set of magnetic resonance-compatible goggles (Nordic Neurolab, Bergen, Norway). An integrated infrared eyetracking camera was also used (ViewPoint Eye Tracker, Arrington Research, Scottsdale, AZ) to monitor and record eye movements inside the scanner. Eye videos were recorded for offline analysis. One of six prerecorded wake-up calls (e.g., "Open your eyes", "Please respond") was delivered whenever participants either missed three consecutive targets or had their eyes fully closed for three consecutive trials.

RT Data

Other than those that were excluded following wake-up calls, all other trials were counted as hits. RTs ranged from 173 to 2,450 ms, whereas false alarms were not analyzed.

We used 800 ms (approximately twice the mean RT in the rested state) as the threshold to define behavioral lapses instead of the 500-ms lapse cutoff commonly used in PVT analyses.[2,12] This different threshold was used because our response grip system resulted in slower responses than those observed in the PVT data (422 ± 94 ms versus 257 ± 32 ms, $t(15) = 7.88$, $P < 0.005$), likely a result of the mechanical properties of the switches on the grip system as well as their use in the supine position.

Within-run time-on-task analyses on eye closure and reaction times were conducted by first segregating the data into four 2.5-min bins. So that nonresponses could be represented for this set of analyses, RTs for nonresponses were set to 6 sec, representing the mean and median SOA between trials. Note that our analyses were performed on median RTs, so the exact value chosen for the nonresponse RT does not affect our conclusions.

Eye-Scoring Procedure

Video clips (30 frames/sec) spanning -450 ms to 1,350 ms (60 frames) around each auditory stimulus were extracted and were rated by two independent scorers. These raters assigned eyescore (ES) values between 1 (eyes fully closed) and 9 (eyes fully opened) for each clip. This method provided a finer-grained measure of eye closure compared to the discrete eyes-opened or eyes-closed rating used previously.[12] To reduce the likelihood of an experimenter-driven increase in eyes-open trials during TSD, trials occurring within 10 sec after a wake-up alarm were excluded from analysis. To ensure that there was no systematic bias in detection of time-on-task effects, the video segments of each subject were randomly shuffled during the review process such that a rater had no idea if an earlier or later event was being viewed.

For statistical analyses, the original 9 ES categories for each state were collapsed into 3 ES bins (ES 1-3 indicating trials that occurred with the eyes mostly closed, ES 4-6 with the eyes semiopen, and ES 7-9 with the eyes mostly open) and then transformed to $\sqrt{n}+\sqrt{n+1}$,[12,29] where n = number of trials in each ES bin (Figure 1). Most analyses were performed using repeated-measures analyses of variance (ANOVA) using SPSS 20.0 for Macintosh (SPSS, Inc. Chicago, IL). Where the Mauchly Test of Sphericity indicated that the assumptions of sphericity were violated, Greenhouse-Geisser corrections for degrees of freedom were applied.

A total of 11,104 RW and 10,606 TSD video segments were assessed by each of two raters and the average score ES was entered for each segment. The mean intraclass correlation coefficient (ICC) (2,1)[30] was 0.82.

Table 1—Means and standard deviations (in parentheses) of response time metrics in rested wakefulness and TSD

RT Metric	RW	TSD	*t*-value
Mean RT (ms)	430 (81)	526 (85)	-6.92***
StdDev RT (ms)	122 (67)	222 (69)	-7.30***
1/Mean RT (1/s)	2.57 (0.4)	2.25 (0.34)	4.93***
Fastest 10% (ms)	313 (39)	334 (35)	-4.07***
Slowest 10% (ms)	741 (236)	1120 (265)	-7.20***
Hit Rate (%)	99 (2.5)	87 (10.5)	4.51***

***P < 0.005. RW, rested wakefulness; RT, response time; StdDev, standard deviation; TSD, total sleep deprivation.

RESULTS

Effect of State on Response Time and Eye Closure Scores

Participants had significantly higher self-rated sleepiness in the TSD session compared with the RW session (KSS; 7.9 ± 1.4 versus 3.4 ± 1.4, t_{18} = 10.25, P < 0.001). There were significant effects of state on several measures of response time, in agreement with previous reports involving visual stimuli.[26,31] TSD resulted in slower mean and median RTs, lower reciprocal RTs, more nonresponses, more variable response times (as assessed by standard deviation of RTs) and longer 10% slowest/fastest RTs (Table 1). Eye closure scores (ES) also showed significant main effects of state, whereas TSD was associated with lower and more variable ES (Table 2).

The trial frequency within each ES category for each state was calculated for all trials, lapses as defined by the combination of trials where RT > 800 ms and trials with no response, and the fastest 10% of trials (Figure S1). However, for all statistical analyses, the collapsed and transformed data (Materials and Methods section) shown in Figure 1 was used instead.

Taking all trials into consideration, we found a significant difference in the frequency distribution of eye-closure scores across state, evidenced by the significant interaction between state and ES bin ($F_{1.37,24.7}$ = 13.99, P < 0.005). In RW, *post hoc t*-tests (Bonferroni correction adjusted for 9 planned comparisons) indicated that eyes-open trials were more frequent than eyes-closed trials (comparisons across ES bins, P < 0.005 except marginal effect of ES 1-3 versus ES 4-6 at P = 0.014). Conversely, the distribution of trials sorted by ES bin was relatively uniform in TSD (P > 0.05). Stated differently, TSD resulted in an increase in trials belonging to lower ES bins (ES 1-3) and a decrease in trials belonging to higher ES bins (ES 7-9; P < 0.005) without affecting intermediate eye-closures (ES 4-6; P = 0.11).

Considering the number of lapses in each ES bin as a function of state, there was a significant state by ES interaction ($F_{1.32,23.7}$ = 28.56, P < 0.005). *Post hoc t*-tests revealed that in TSD, there was a graded relationship between ES and lapses whereby greater degrees of eye closure predicted a higher number of auditory lapses (P < 0.005). In contrast, in the RW state, no pairwise comparisons of lapses in different ES bins showed a significant difference. There were significantly more lapses in ES 1-3 and ES 4-6 (P < 0.005) during TSD compared with RW, and a marginal difference for ES 7-9 (P = 0.09).

Table 2—Means and standard deviations (in parentheses) of ES metrics in RW and TSD

ES Metric	RW	TSD	*t*-value
Mean ES (1-9)	7.12 (1.39)	5.09 (1.58)	5.43***
StdDev ES	1.18 (0.56)	1.96 (0.55)	-5.33***

***P < 0.005. RW, rested wakefulness; RT, response time; StdDev, standard deviation; TSD, total sleep deprivation.

These findings suggest that eye closure scores are less predictive of lapses in the RW state than in TSD. However, the base rate differences (e.g., very few ES 1-3 trials in RW) between states warranted additional analysis. An ANOVA using the ratio of lapses to the total number of trials in an ES bin was conducted (Figure S2). 7 subjects who had at least 10 trials in each ES bin in both states contributed to this analysis. There were significant main effects of state ($F_{1,6}$ = 21.04, P < 0.005) and ES bin ($F_{1.06,6.33}$ = 16.6, P < 0.01) on these ratios, as well as an interaction between state and ES bin ($F_{2,12}$ = 34.4, P < 0.005). In TSD there were significantly more lapses with lower ES (P < 0.005) but in RW, the *post hoc t*-tests showed only borderline differences in lapse rate across different eye-closure scores (marginal difference between ES 1-3 and ES 4-6, P = 0.05). Lapses in TSD were qualitatively more severe with increasing eye closure, as indicated by the percentage of lapses due to nonresponses (ES 1-3: 36% ± 4.4, ES 4-6: 8.9% ± 2.2, ES 7-9: 4.0% ± 2.1 [mean ± standard error of the mean]; one-way ANOVA: $F_{1.14,20.5}$ = 26.82, P < 0.001). An analysis involving all 19 subjects using a general linear mixed model with PROC MIXED in SAS 9.2 (SAS Institute, Cary, NC), which permits the inclusion of subjects with missing data, was additionally conducted. The details and results of this procedure are included in Figure S3.

The relevance of eye closures to responses to auditory stimuli was complemented by an analysis of the fastest 10% of trials. In RW, the distribution of fastest trials with respect to eye closure (Figure 1C) paralleled the frequency distribution of all trials (Figure 1A). In contrast, a disproportionate number of the fastest trials during TSD occurred when the eyes were open (one-way ANOVA; $F_{2,36}$ = 14.26, P < 0.005).

Time-On-Task Effects on Eye Closure and RT

Within each 10-min run, there were main effects of state ($F_{1,18}$ = 15.89, P < 0.005) and experimental duration ($F_{1.96,32.3}$ = 28.28, P < 0.005) on eye closure (ES scores) and also a significant state-by-duration interaction ($F_{2.01,36.2}$ = 9.18, P < 0.005; Figure 2A). An increase in the degree of eye closure was thus more pronounced over time during TSD compared to RW.

To investigate the effect of run duration on response times, these were transformed to 1/RT to minimize the effect of the long tail typical in RT distributions.[21] Main effects of state ($F_{1,18}$ = 26.01, P < 0.005) and run duration ($F_{3,54}$ = 2.84, P < 0.05) were present but there was no significant interaction ($F_{3,54}$ = 0.05, not significant; Figure 2B). Between-run effects were not significant for either response times or eye closure, showing that even a brief break of approximately 1 min between runs may help attenuate the time-on-task effect.

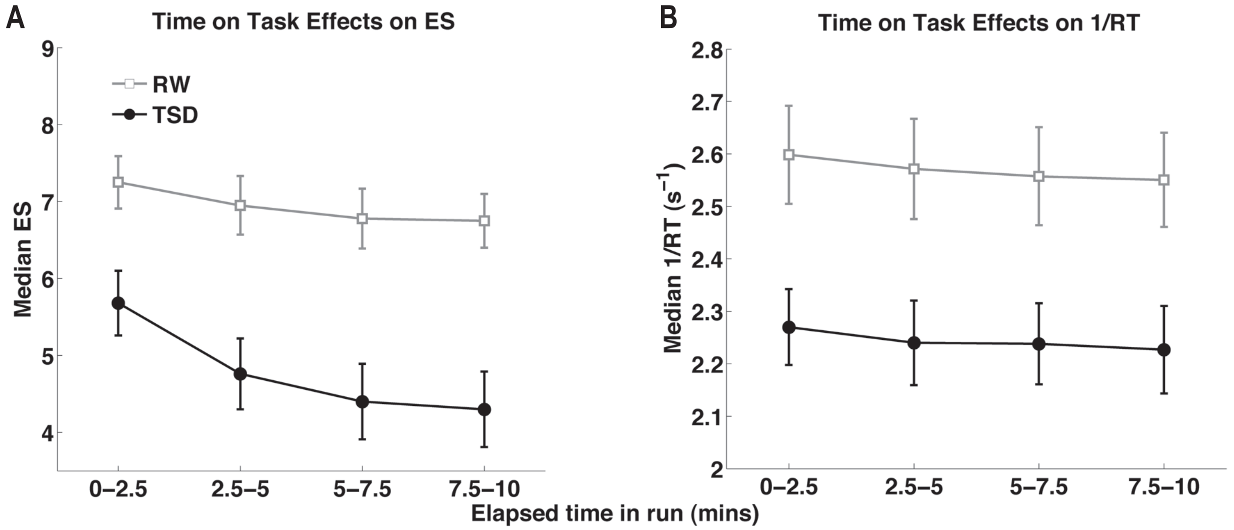

Figure 2—Time-on-task effects on **(A)** eyescore and **(B)** 1/RT in RW (open squares) and TSD (filled circles) within a run. RTs for non-responses were set to 6 sec, representing the mean and median SOA between trials. Error bars represent standard error of the mean. RT, response time; SOA, stimulus onset intervals; TSD, total sleep deprivation.

Table 3—Means and standard deviations (in parentheses) for RT and ES metrics in TSD for Less Vulnerable (LV) and More Vulnerable (MV) participants

RT/ES Metric	LV	MV	*t*-value
Hit Rate (%)	96 (3.2)	79 (8.1)	5.93***
Lapses [a] (%)	12 (10.5)	29 (9.5)	-3.59***
Mean RT (ms)	504 (102)	544 (70)	n.s.
StdDev RT (ms)	185 (70)	285 (54)	-2.47*
Mean ES (1-9)	4.66 (1.36)	5.26 (1.72)	-n.s.
StdDev ES	1.64 (0.54)	2.32 (0.33)	-3.22***

[a] Includes nonresponses and RTs > 800 ms. *P < 0.05, ***P < 0.005. RW, rested wakefulness; RT, response time; StdDev, standard deviation; TSD, total sleep deprivation.

Differences Among Persons More and Less Vulnerable to Sleep Deprivation

A median split was used to separate participants according to hit rate (defined as percentage of trials with a response excluding trials occurring immediately after a wake- up alarm) in the TSD condition. The better 9 performers were classified as less vulnerable (LV) and the poorer 9 as more vulnerable (MV). The median subject was excluded. Histograms of ES frequency for these two groups are shown in Figure S4. Although mean ES ratings were not significantly different between the groups, the more vulnerable group exhibited higher within-subject variance in both RT and ES metrics in TSD (Table 3). This result was not merely a consequence of their being alerted more often than the LV group, as trials following a 10-sec window after a wake-up call were removed from all analyses. Although we divided our sample into two groups for clearer data presentation, we found that vulnerability, as indexed by hit rate, varied evenly across the sample. This feature of the data is shown in a scatterplot of hit rate versus standard deviation of ES, two measures that were negatively correlated (r(16) = -0.69, P < 0.01; Figure S5).

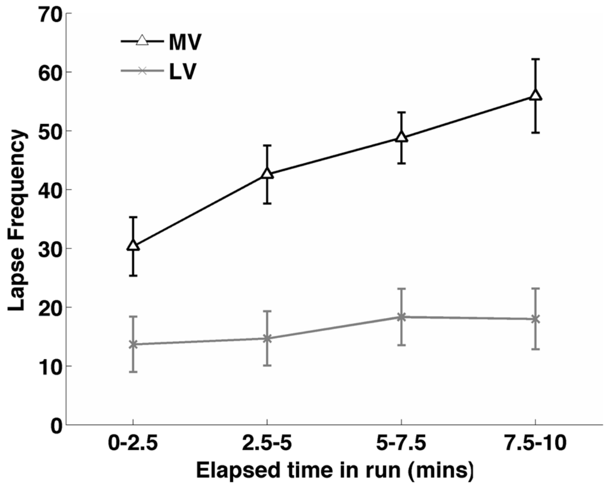

Figure 3—Time-on-task effects on lapse frequency for less vulnerable (LV; gray crosses) and more vulnerable (MV; black open triangles) participants within a run in total sleep deprivation. Error bars represent standard error of the mean.

During TSD, time-on-task effects on lapse frequency differed between the groups. This was shown using a mixed-design ANOVA with duration as the within-subject factor and vulnerability the between-subject factor (Figure 3). Critically, there was a significant interaction between duration and vulnerability ($F_{3,48} = 3.77$, P < 0.05). Experiment duration increased lapse frequency in the MV group ($F_{3,24} = 17.96$, P < 0.005; linear contrast : $F_{1,8} = 49.8$, P < 0.005) but not the LV group ($F_{3,24} = 2.073$, not significant)

DISCUSSION

We used an auditory vigilance task paradigm and continuous measurement of eye-closure scores in order to probe the relationship between eye closures and performance in different states. This analysis enabled us to study the integrity of sensory signal detection in sleep-deprived persons without the eyelids acting as a physical barrier to perception. We found that for the average participant, in contrast to the preponderance of eyes-open trials when participants were well rested, different degrees of eye closure were relatively uniformly distributed during sleep deprivation. In this latter state, the frequency of lapses (including nonresponses to auditory targets) increased dramatically with greater degrees of eye closure. Interestingly, participants who were relatively more vulnerable to the effects of TSD had greater variance in degree of eye closure compared to less vulnerable participants, speaking to the notion of 'state-instability'[26] in vulnerable individuals.

Eyelid Closure Strongly Predicts Lapses in TSD: A Reflection of Microsleeps

The substantial decrease in the frequency of lapses as eye-closure score increases appears to follow a hyperbolic or decaying exponential function. Clearly, when the eyes were fully or mostly closed, performance was at its poorest. This supports the rationale for selecting 80% eye closure as a practical criterion for denoting high risk of lapsing and extends it beyond the visual domain.[10]

The sharply reduced behavioral responsiveness associated with complete eye closure in TSD is consistent with many trials representing microsleeps. To the extent that microsleeps are similar to sleep proper, previous sleep research provides an explanation for our behavioral effects. For example, the elevation of sensory thresholds in sleep[19] is thought to result from reduced transmission of sensory information to higher cortical areas. Higher cortical processing of sensory inputs appears necessary for speedy responses to target stimuli.[32] During deep sleep, higher cortical areas are isolated from brainstem, subcortical, or primary sensory cortical inputs.[33] Even in lightly sedated patients, higher-order aspects of speech processing in frontal cortex are attenuated despite the preservation of perceptual responses to speech sounds in the primary auditory cortex.[34]

Early latency auditory-evoked responses generated in the acoustic nerve and in the brainstem are relatively well preserved in the sleep-deprived state, but midlatency and later potentials reflecting thalamocortical processing are delayed and attenuated.[32] The slowing of behavioral responses correlates with the extent to which later potentials are delayed or attenuated.

Another perspective on eye closures merits discussion: even in fully awake persons, blinks are known to transiently impair visual task performance while attenuating activation of visual cortex and areas that mediate top-down control of attention.[35-37] Blinking also transiently engages the default mode network, which is associated with mind wandering and loss of task engagement.[38] Such results suggest that blinking also may be associated with diminished responsiveness to nonvisual stimulus modalities. If so, it is possible that blinks during TSD may have the same relationship to behavior and brain activity as blinks in the rested state, with larger effects due to SD's more frequent and longer-duration blinks. Alternatively, blinks during SD may be an integral and indicative part of falling asleep, where a broader, cross-modality attenuation of sensory processing occurs in conjunction with disruptions to visual processing. The data in the present study seem to suggest the latter explanation, but clearly, this question should be further researched.

Eyes-Open Lapses to Auditory Stimuli: A Reflection of Mind-Wandering?

Behavioral lapses with eyes partially open can occur in both sleep-deprived and well-rested persons (Figure 1B).[39,40] A number of eyes-open lapses have been shown to be a result of deliberate distraction.[12] Other lapses, such as those in the current study, have been attributed to transient 'daydreaming'[41] or 'mind-wandering'.[42] Functional imaging studies indicate that performing tasks involving external stimuli involves activation of networks mediating attention as well as deactivation of an internally oriented 'default mode network' that is active during internally oriented cognition.[43-45] Mind wandering without awareness, the kind that gives rise to lapses, expectedly increases activity within the default mode network but in addition, there is activation of the attention network.[46] This decoupling of networks occurs during 'Stimulus Independent Thought' where a shift to internally directed thinking occurs, taking one away from the stimulus at hand. Mind wandering of this sort would be expected to predominate in RW whereas microsleeps/sleep would predominate in TSD. However, a direct comparison between behavior, oculomotor variables, and fMRI across state remains to be conducted. Such a study could contribute to our understanding of why behavioral and physiological (oculomotor and electroencephalograph) measures individually predict drowsiness but may be uncorrelated.[10]

Time-on-Task Effects of Eye Closure on Auditory Responses

Continuous engagement on an attention-demanding task leads to declines in performance, such as increased lapse rates and longer reaction times. Such time-on-task effects are also exacerbated by sleep deprivation.[21] Here we demonstrated that eye closure also shows time-on-task effects that are more severe during sleep deprivation.

In previous research comparing auditory and visual PVT performance in sleep-deprived persons, state-related slowing in response time was significant in both modalities.[31] However, the shift in auditory PVT response times across state (RW-TSD) was smaller than the corresponding in visual PVT response times, underscoring the utility of using auditory signals as alarms.[26,31]

In addition, we found that an approximate 1-min break between experimental runs was sufficient to return performance to almost baseline levels for that state. Regular breaks have been demonstrated to have a positive, short-term effect on subjective alertness and performance,[47] although there has been no study to date investigating an optimal break duration. This could be expected to be dependent on the length and type of task performed.

Vulnerable Participants Display Increased Variability in RT and Eye Closure

The increased variance in both eye closures and response times in subjects more vulnerable to sleep deprivation speaks to heightened state-instability. Increased variation in response times is a robust finding across several studies involving TSD.[3] Increased variance in eye closure has been observed with drowsy drivers,[13] and the findings here are in agreement. In addition, the more vulnerable sleep-deprived participants show greater variance in eye closure. It would appear that these participants exert effort to counter sleepiness (more trials with eyes fully open), but that such effort intermittently fails, resulting in microsleeps (more trials with eyes closed and increased lapses).

CONCLUSION

Eyelid closures are a strong predictor of auditory task disengagement in the sleep-deprived state, but these may be less relevant in well-rested persons who display a limited range of eye closures. Individuals relatively more impaired in auditory vigilance tasks when sleep deprived display oculomotor evidence for greater state instability, with higher variance in eye closure.

DISCLOSURE STATEMENT

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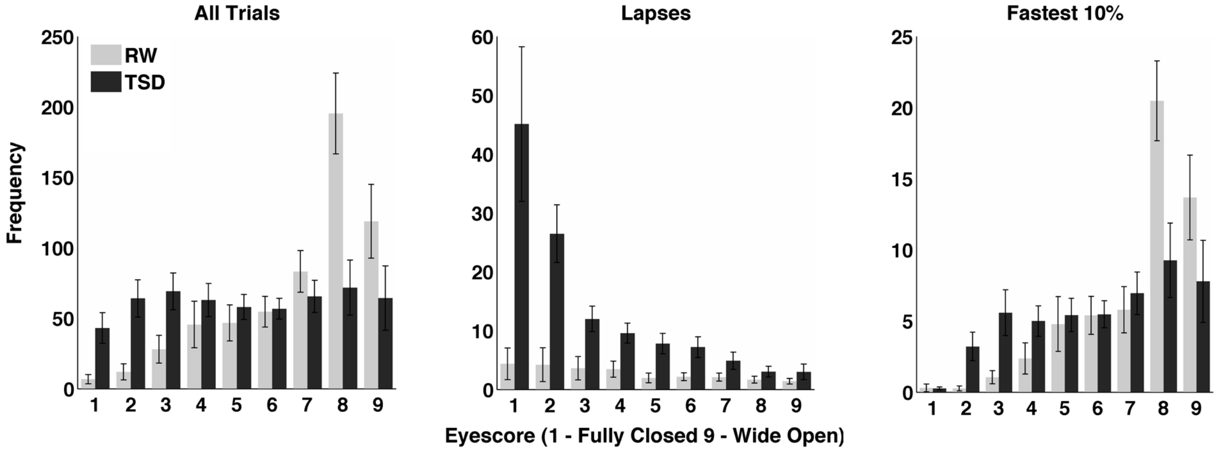

Figure S1—Histograms of ES frequency in rested wakefulness (RW; light gray bars) and total sleep deprivation (TSD; dark gray bars) for 19 participants grouped by RT behavior – all trials, lapses, and fastest 10%. Error bars represent standard error of the mean.

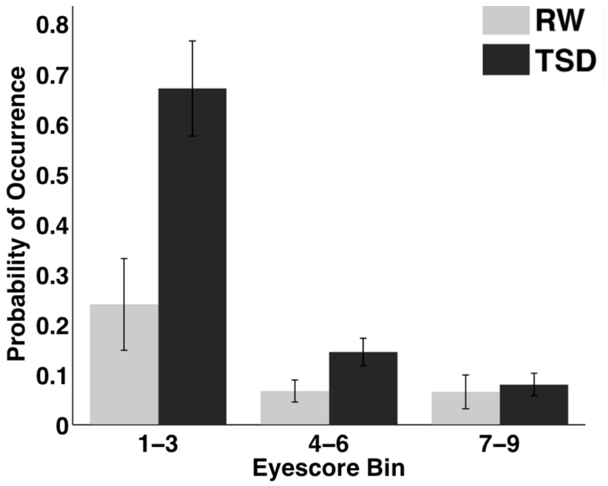

Figure S2—Probability of a lapse (RT > 800 ms or nonresponse) occurring in RW (light gray bars) and TSD (dark gray bars) for a given ES bin. Data are from 7 participants who had at least 10 trials in each bin. For example, if an ES of 1-3 were observed in TSD, the probability of a lapse would be 67%, whereas in RW, this probability would only be 24%. Error bars represent standard error of the mean. ES, eyescore; RT, response time; RW, rested wakefulness; TSD, total sleep deprivation.

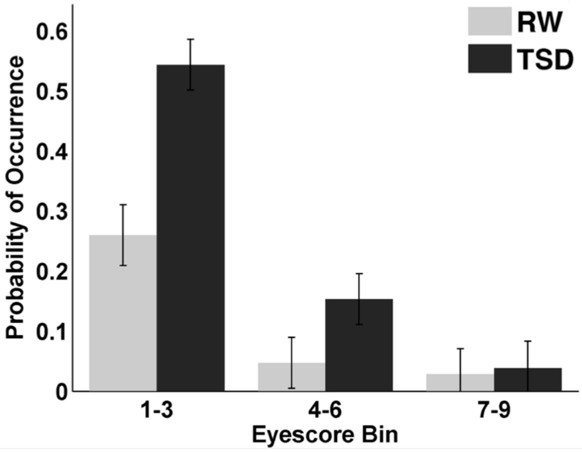

Figure S3—Analysis of lapse probability (RT > 800 ms or nonresponse) conducted on all 19 subjects using a general linear mixed model with PROC MIXED in SAS 9.2 (SAS Institute, Cary, NC). Error bars represent standard error of the mean. This analysis included subjects with missing data, i.e. subjects who had no trials in a particular ES bin. ES bin (1-3, 4-6, and 7-9) was included as a repeated effect with a first-order, autoregressive covariance matrix being specified. State (RW versus TSD), its interaction with ES bin, and visit (first/second laboratory session) were included as fixed effects, and subject as a random factor. Differences of least square means were used to determine significant differences between states and between ES bins at P < 0.05. The results yield similar conclusions as the analyses conducted on the 7 subjects who had at least 10 trials in each ES bin in both states (Figure S2). There were significant main effects of state ($F_{1,16.2}$ = 14.66, P = 0.001), ES bin ($F_{2,67.6}$ = 48.18, P < 0.0001) and interaction between state and ES bin ($F_{2,67.7}$ = 5.86, P < 0.005). However, the results of Figure 2S are reported in the main text because many subjects did not have sufficient trials for calculating a reasonable estimate of lapse probability. For example, a subject who had only 1 trial with ES 1-3 and 1 (or 0) lapse would have a lapse probability of 100% (or 0%). ES, eyescore; RT, response time; RW, rested wakefulness; TSD, total sleep deprivation.

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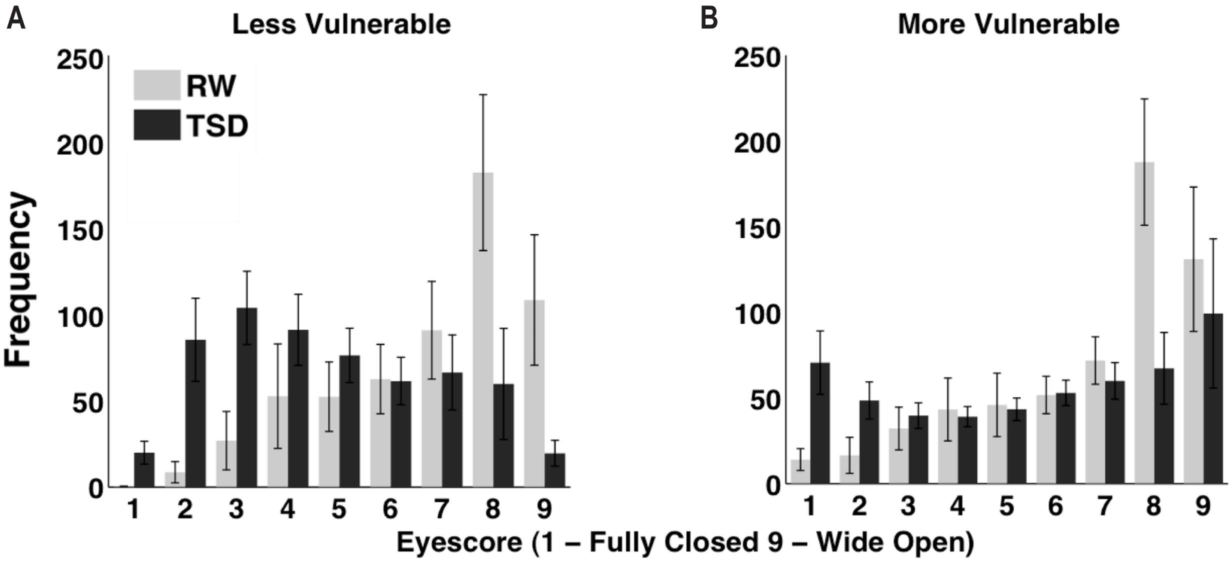

Figure S4—Histograms of ES frequency for **(A)** less vulnerable (LV) and **(B)** more vulnerable (MV) participants across all trials in RW (light gray bars) and TSD (dark gray bars). Error bars represent standard error of the mean. Note that although the distribution of scores in both groups was similar in the RW state, they were differentiated in TSD. The MV participants show a U-shaped distribution of ES in TSD, consistent with heightened state-instability and increased effort to maintain wakefulness, whereas the LV group shows an inverted-U distribution. ES, eyescore; RW, rested wakefulness; TSD, total sleep deprivation.

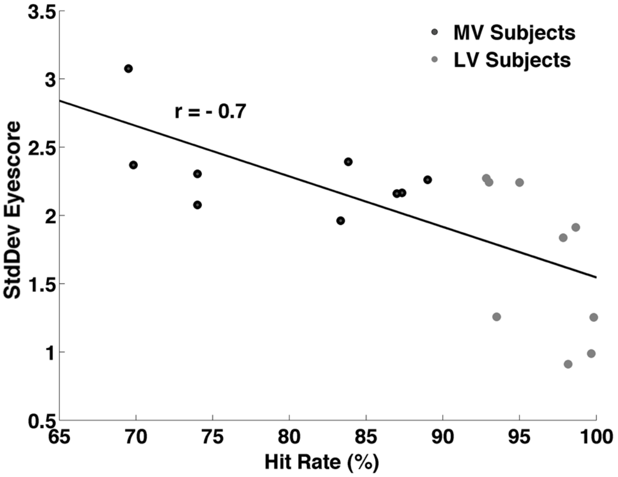

Figure S5—Scatterplot of the relationship between hit rate (%) and standard deviation of eyescore after TSD. More and less vulnerable subjects are represented by black and gray filled circles, respectively. Pearson correlation was significant ($P < 0.01$). StdDev Eyescore, standard deviation of eyescore; RW, rested wakefulness; TSD, total sleep deprivation.

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