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An examination of the association between chronic sleep restriction and electrocortical arousal in college students

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HIGHLIGHTS

- Chronic sleep deficits across an academic semester impair vigilant attention.
- Changes in circadian rhythm activity and average daily sleep are each associated with changes in cortical arousal.
- Very small changes in sleep have a profound effect on neurocortical functioning.

ABSTRACT

Objective: The deleterious neurocognitive effects of laboratory-controlled short-term sleep deprivation are well-known. The present study investigated neurocognitive changes arising from chronic sleep restriction outside the laboratory.
Methods: Sleep patterns of 24 undergraduates were tracked via actigraphy across a 15-week semester. At the semester beginning, at a midpoint, and a week before finals, students performed the Psychomotor Vigilance Test (PVT) and cortical arousal was measured via event-related potentials (ERP) and resting state electroencephalography (EEG).
Results: Average daily sleep decreased between Session 1 and Sessions 2 and 3. Calculated circadian rhythm measures indicated nighttime movement increased and sleep quality decreased from Sessions 1 and 2 to Session 3. Parallel to the sleep/activity measures, PVT reaction time increased between Session 1 and Sessions 2 and 3 and resting state alpha EEG reactivity magnitude and PVT-evoked P3 ERP amplitude decreased between Session 1 and Sessions 2 and 3. Cross-sectional regressions showed PVT reaction time was negatively associated with average daily sleep, alpha reactivity, and P3 changes; sleep/circadian measures were associated with alpha reactivity and/or P3 changes.
Conclusions: Small, but persistent sleep deficits reduced cortical arousal and impaired vigilant attention.
Significance: Chronic sleep restriction impacts neurocognition in a manner similar to laboratory controlled sleep deprivation.

1. Introduction

Sleep plays an essential role in supporting effective cognitive processing (Doran et al., 2001; Fallone et al., 2001; Taras and Potts-Datema, 2005; Kong et al., 2012), yet sleep deprivation and sleep restriction are very common conditions for the general populace (Centers for Disease Control and Prevention, 2013). In fact, thirty percent of adults report getting less than the recommended 7–8 h of sleep per night according to a 2007–2008 survey by the Center for Disease Control (CDC).

Considerable research has examined the effects of total sleep deprivation (TSD) on cognitive processes such as working memory, executive functioning, learning, and selective attention (Harrison

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and Horne, 2000; Smith et al., 2002; Trujillo et al., 2009; Tucker et al., 2010; Maddox et al., 2011). Of particular importance, and a domain of considerable research, is the effect of TSD on vigilance – defined as "the ability of organisms to maintain their focus of attention and to remain alert to stimuli over prolonged periods of time" (Warm et al., 2008, p. 433) – because attentional deficits reliably impact many high-level aspects of cognition (Lim and Dinges, 2008; Jung et al., 2011; Jugovac and Cavallero, 2012). Multiple controlled studies have shown that TSD is fundamentally related to a decrease in the ability to sustain attention, as demonstrated by changes in performance on the psychomotor vigilance task (PVT; Lim and Dinges, 2008; Franzen et al., 2008; Hoedlmoser et al., 2011). In addition to its use in studies of TSD, the PVT has also been used in monitoring effects of sleep restriction in controlled laboratory settings (Dinges et al., 1997; Drake et al., 2001; Vgontzas et al., 2004). For example, in a study by Belenky et al. (2003) participants were split into four different cohorts who experienced various levels of sleep restriction over a 7-day period followed by a 3-night recovery period. Participants were tested using the PVT four times each day and the cohort with the greatest sleep restriction (3 h a night) showed the greatest increases in response time. The less restrictive cohorts of 5 and 7 h a night showed an initial decrease in their performance, which eventually leveled out below their initial speed. During the recovery period, the 5-h and 7-h cohorts did not return to baseline. While the 3-h cohort did improve their reaction times, they also did not show a full rebound, with performance leveling off at the same speed of the 5- and 7-h recovery scores. Therefore, the PVT has been shown to serve as an accurate and reliable measure of vigilance and is the measure most often used in sleep research studies (Dinges and Powell, 1985; Balkin et al., 2004).

Despite its widespread use in sleep research, less is known about the neural basis of performance changes in the PVT. One previous study (Hoedlmoser et al., 2011) found TSD-related PVT performance impairments to be accompanied by decreased activation of event-related electroencephalographic (EEG)-based responses including the early visual event-related potential (ERP) P1 component and delta/theta-band intertrial EEG phase variability. This finding of decreased ERP responses during PVT performance under conditions of TSD is consistent with the results of several previous electrophysiological studies of the effects of sleep deprivation on attention, cognition, and perception (see Trujillo et al., 2009, for a brief review).

Sleep research to date has rarely combined examinations of sleep restriction with neurocognitive measures over extended periods of time in real-world settings. Hence it is unknown the degree to which individuals can adapt to more chronic forms of sleep restriction and whether performance measures such as the PVT and scalp recorded EEG can be sensitive to variations in real-world sleep patterns. This was the primary goal of the present study – to examine the neurocognitive effects of chronic sleep restriction using the PVT in conjunction with EEG measures in a group of normally functioning college students over a period of approximately 15 weeks. Aside from being a convenience sample, college students, and young adults in general, suffer some of the worst sleep restriction (Bonnet and Arand, 1995; Carpenter, 2001; Buboltz et al., 2001). A study by Coren (1994) showed that only about one-third of young adults do not suffer from some sort of sleep disturbance. Lack (1986) observed 'difficulty falling asleep' as the most-often reported sleep issue of approximately 18 percent of the college student sample. Fifty percent of this same group also reported getting insufficient sleep and needing at least 30 additional minutes of sleep time in order to feel rested (Lack, 1986). Clearly, student populations are not receiving ample rest and are thus a good cohort to use when examining the neurocognitive effects of sleep patterns across extended periods of time.

In the present study, student sleep patterns throughout a single school semester were assessed via actigraphy to provide a quantitative continuous measure of sleep/wake activity (Littner et al., 2003). At three intervals throughout a semester (beginning, middle, end), participants performed the PVT while scalp ERPs were recorded. Additionally, we investigated changes in general cortical arousal using a measure of resting state alpha reactivity of the EEG that has previously been shown to be sensitive to sleep loss (Kornguth et al., 2013).

2. Methods

2.1. Participants

Twenty-eight undergraduate students at the University of Texas at Austin were paid for participating in our study (10 males, $M = 20.2 \pm .4$ years). One participant opted to drop out during the first third of the study and so was not included in the analyses. Three participants were excluded from the analyses due to missing large portions of actigraph data. Thus, a total of twenty-four participants were used for all analyses. All participants were right-handed and had no history of neurological or psychological disorders, including sleep disorders. Criteria for participation in this study included a GPA (grade point average) cut-off of above 3.0 and at least 1 year as an undergraduate, attended at the University of Texas. The reason for these criteria was to insure that the primary determinant of the pattern of sleep behavior was successful functioning as an undergraduate student. All participants gave informed consent before testing. This study was approved by the institutional review board at the University of Texas.

2.2. Procedure

Participants were recruited at the beginning of the academic school semester, and after an initial phone screening, attended their first session. At this session, questionnaires including the PANAS (Positive and Negative Affect Schedule), ERQ (Emotion Regulation Questionnaire), CES-D (Center for Epidemiologic Studies Depression Scale), PSQI (Pittsburgh Sleep Quality Index), and a health and demographics questionnaire were completed. We have previously used these questionnaires in normal functioning college students (Vanderlind et al., 2014) and they are widely accepted for use in a non-clinical setting (Crawford and Henry, 2004). None of these measures were used as rejection criteria, as participants had already been screened using a phone survey.

The participants then underwent 10 min of resting state EEG recording while sitting quietly in a comfortable padded chair (5 min eyes open and 5 min eyes closed interleaved in 1-min intervals; eyes open/closed order was balanced across participants). Next, the participants underwent an approximate ten-minute session of EEG recording during performance of the psychomotor vigilance task (PVT; Dinges and Powell, 1985). The PVT is a high-signal load reaction time test in which participants attended to a small fixation cross at the center of a computer screen. At random intervals (2–10 s inter-trial intervals), a bright millisecond timer appeared at the center of the screen. The timer stimulus subtended ~2.35° (w) × .75° (h) of visual angle at a viewing distance of 100 cm. Upon detection of the counter stimulus, participants responded as rapidly as possible via button press with their dominant hand. A participant's response stopped the counter from updating and the final counter value, corresponding to the participant's RT in milliseconds, provided performance feedback for that particular trial. After a one-second exposure duration, the final counter value was replaced by a new fixation cross. Participants were given 30 s to make a response before the computer automatically aborted a trial.

Each PVT run was composed of 100 trials over an approximate 10-minute period.

After completing the PVT in the first session, participants were fitted with a Motionlogger Actigraph (Ambulatory Monitoring, Ardsley, NY, USA) an accelerometer-device worn on the wrist that measures gross motor movement provides a quantitative continuous measure of sleep/wake activity (Littner et al., 2003). Participants were requested to wear the actigraphs at all times throughout the semester unless engaging in activity that could potentially damage the device and/or that is otherwise inappropriate to wear the device (e.g., bathing and water activities, sexual activity, extreme sporting activities). Participants were also instructed to keep a daily sleep journal either on a paper spiral notebook or through RedCap-an online software system for recording and analyzing questionnaires completed by participants (Harris et al., 2009). The paper sleep journals and Redcap were used to record self-identified time it took to fall asleep, number and time period of nightly awakenings, self-reported quality of sleep, time at which they awoke, plus any time periods during which they removed the actigraph from their wrists.

After a period of approximately 6 weeks (which coincides with the middle of the academic semester), participants returned for a second session of EEG/PVT assessment and to download the actigraph data and reset the watch. Once again, the PSQI, PANAS, and CES-D were completed during this mid-semester session. A final session approximately 6 weeks later (at the end of the academic semester) included the same EEG/PVT, data download and collection of behavioral measures.

2.3. Actigraphic recording and data reduction

Motionlogger Actigraphs (Ambulatory Monitoring, Inc., Ardsley, NY) were collected from participants during the second and third laboratory visits. Records from the devices were downloaded using the ambulatory monitoring software. Actigraph recordings were made in zero-crossing mode (ZCM) with 1 min epochs. These data were then screened by comparing the reported sleep journals with the movement recorded by the accelerometer. Using these journals, time spans when the actigraph was reportedly removed were deleted from the ZCM channel. The actigraph was used as the ultimate measure and time spans were deleted to coincide with the self-recorded lack of movement. The life or temperature channels were the method used to guide when the actigraph might have been removed if there was no sleep journal entry for that day. After the removal of minutes during which the actigraph was not worn, minutes during which a participant was asleep or awake were determined from the remaining data based on the ZCM channel using the Cole-Kripke PCD ZCM algorithm via Action 4 software (Ambulatory Monitoring, Inc., Ardsley, NY) (Cole et al., 1992; Jean-Louis et al., 2001).

Two sets of sleep measures were computed from the actigraph data. First, average daily sleep per week was quantified as the mean daily amount of sleep (in minutes) indicated by the actigraph between the self-reported wake times (via sleep journal) from one day to the next; if the sleep journal entry was missing, wake times were interpreted based on the activity of the accelerometer. Second, the continuous collection of actigraph data provides the ability to calculate validated measures of circadian rhythms that correlate with core body temperature and reliably match the circadian period of polysomnography data (Pollak et al., 2001; for review see: Ancoli-Israel et al., 2003). Circadian activity rhythms were calculated by fitting the data from the ZCM channel to a five-parameter extended cosine model (Martin et al., 2000). This model approximates the consistently observed square wave pattern of activity data (Marler et al., 2006) and is an effective tool to quantify changes in circadian activity rhythms across time (Savard et al., 2009; Ancoli-Israel et al., 2002; Tranah et al., 2011). Using non-linear least squares, parameters were estimated from the model over one-week intervals (see below). The outcome of this analysis captures the weekly rhythms of circadian activity. The measures of interest were circadian amplitude-the peak of the rhythm, circadian minimum, and the robustness of the circadian rhythm (F-statistic). Circadian amplitude is the difference in activity between the peak and nadir, representing the strength of the rhythm (measured in arbitrary units of activity [counts/activity]). The circadian minimum is the lowest point on the curve and higher values indicate more activity during the night. The F-statistic measures the goodness of the extended cosine fit with a larger value signifying more rhythmic or robust circadian rhythms.

Average daily sleep and circadian activity rhythm were assessed over a one week period for each testing session.[2] Because the actigraphs were only received before the initial EEG session by 9 of the 24 participants, sleep measures for Session 1 were calculated using data acquired over the week directly following the first testing session, whereas sleep measures for Sessions 2 and 3 were calculated using data acquired over the week prior to each testing session. This choice was justified by the finding that average daily sleep and circadian activity remained fairly stable across the weeks immediately before and after the first two testing sessions (see Appendix A).

2.4. PVT behavior data reduction

In order to eliminate false starts and behavioral lapses, we restricted analysis to correct trials with response times (RTs) >200 ms and <500 ms; these cutoffs were based on the known limits of human visual processing speed and previous studies utilizing the PVT (Dinges and Powell, 1985; Fabre-Thorpe et al., 2001). A total of 7.8 ± 1.2% of trials with RTs outside the specified limits were rejected. Mean RTs were computed from these trimmed values for each participant and PVT session. We also analyzed the proportion of lapse trials (RTs > 500 ms) in each session.

2.5. EEG recording and data reduction

Sixty-seven channels of DC EEG were recorded both during the resting task and during the PVT from active Ag/AgCl electrodes mounted in a BioSemi electrode cap (BioSemi B.V., Amsterdam, The Netherlands) placed on the participants' heads (Fig. 1). Vertical eye blinks and saccades were measured via two additional electrodes placed on the inferior orbits of both eyes, whereas two other electrodes placed at the lateral canthi measured horizontal saccadic activity. All channels were amplified using the BioSemi Active II amplifier system in 24 bit DC mode at an initial sampling rate of 2048 Hz (400 Hz bandwidth) decimated online to 256 Hz. EEG signals were recorded with respect to a common mode sense active electrode placed between sites PO3 and POZ. Half-cell potentials between the electrode, recording gel, and skin were kept between ±40 mV, following standard recommendations for the Active II system.

Continuous EEG data were imported off-line into the MATLAB computing software environment (The Math Works, Inc., Natick, MA, USA) using the EEGLAB toolbox (Delorme and Makeig, 2004) for MATLAB, where all subsequent analysis was performed via inhouse scripts that utilized EEGLAB functions. The continuous EEG data for the resting task was divided into six hundred

[2] Due to recording errors, actigraph data were unavailable for one participant for the first testing session and for two participants for the first two testing sessions. The missing average daily sleep per week and circadian rhythm values were estimated for these participants/sessions from the remaining data using the Missing Values Analysis Expectation Maximization algorithm of the SPSS statistical software.

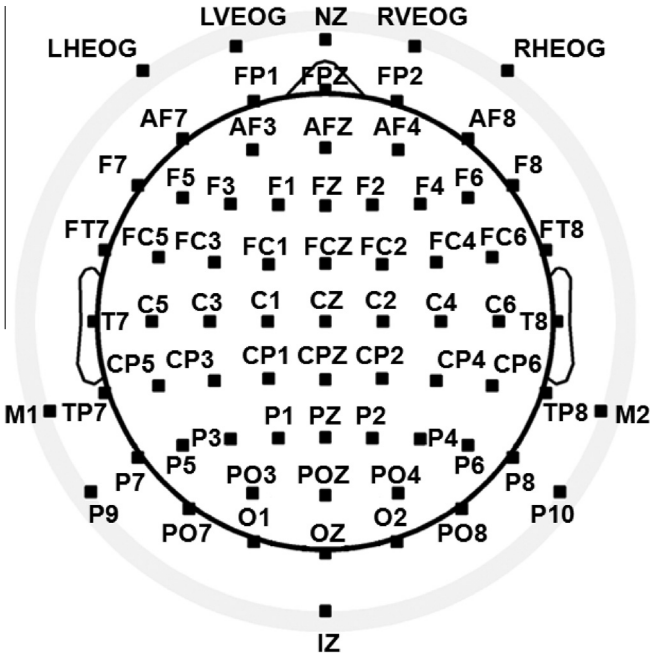

Fig. 1. Extended 10–20 scalp locations of EEG recording electrodes. Note that sites outside the radius of the head represent locations that are below the equatorial plane (FPZ-T7-T8-OZ plane) of the (assumed spherical) head model.

1000 ms epochs with 50% overlap. The continuous PVT EEG data was divided into 2000 ms epochs ranging from −750 ms to 1250 ms with respect to the onset of the counter stimuli; trials with RTs > 200 ms and <500 ms were excluded from further analysis. Next, the EEG trials for both tasks were transformed to a linked-mastoids reference and then artifact scored. A total of 25.5 ± 1.6% and 12.6 ± 1.5% of resting and PVT trials, respectively, were rejected due to muscle, signal, and/or ocular artifacts. Muscle and signal artifacts were removed from the EEG record by visual inspection. Bad EEG channels were replaced using an EEGLAB-based spherical spline interpolation algorithm (Perrin et al., 1987; $m = 5$; 50-term expansion) applied to the remaining channels. The mean number of interpolated channels across participants and sessions was 1.6 ± .19.

Resting EEG trials contaminated with ocular activity were rejected from further analysis based on activity present in additional horizontal and vertical EOG channels computed off-line. The horizontal EOG channel was computed as the bipolar montage of the left and right outer canthi EOG signals; the vertical EOG channel was computed from the bipolar montage of the nasion electrode and the average of the electrodes placed at the inferior orbits. Resting EEG trials containing EOG amplitudes higher than 50 μV or lower than −50 μV (after removal of the constant direct current offset from the EOG signal) were removed from further analysis via an automatic algorithm implemented in MATLAB. Ocular activity during PVT trials was removed using a two-stage rejection/correction procedure (Trujillo et al., 2009) that simultaneously minimizes data loss and the physical/neural impact of ocular activity on the EEG signals. First, trials contaminated with ocular activity in the early stages of the trials (−200 ms to 200 ms with respect to stimulus onset) were rejected in the same manner as described above for the resting EEG. Second, PVT EEG signals were corrected for residual EOG activity outside the above-stated rejection intervals via an adaptive filter-based regression procedure (He et al., 2004) implemented within the Automatic Artifact Removal toolbox v1.3 for EEGLAB and applied to the entire 2 s of each PVT EEG epoch. After elimination of EOG artifacts, the derived EOG channels were removed from the EEG data before further analysis.

Artifact-free resting EEG data were divided into two conditions – Eyes Open and Eyes Closed. Spectral power density (μV^2/Hz) measures were computed for each condition via Fast Fourier Transformation (FFT) with a 256-point Hamming window; on average, 447 ± 10 trials per condition per participant entered into the spectral analysis. The central frequency range of interest was the alpha (8–12 Hz) range, which is known to be highly active during periods of wakefulness in which subjects are resting quietly and are otherwise not cognitively engaged (Niedermeyer, 1999). Larger resting alpha activity occurs when eyes are closed versus open; thus we computed an Alpha Reactivity (AR) index defined as Eyes Closed – Eyes Open resting EEG alpha spectral power density difference at electrode O2 (scalp site of maximal alpha power). The artifact-free PVT counter-locked EEG data were bandpass-filtered between 0.5 and 20 Hz (166 point zero phase shift FIR filter with .08 Hz and 3 Hz transition bands, respectively), truncated from −200 ms to 600 ms with respect to timer onset, and then baseline corrected by subtracting the mean-value over the −200 to 0 ms prestimulus interval for each electrode separately. PVT timer-locked ERPs were then created for each participant and testing session; on average, 87 ± 2 trials per condition per participant entered into the ERP averages. ERP amplitudes were measured for the posterior P1, the central N1, and P3 components by first identifying the component peak responses within the 100–200 ms, 150–250 ms, and 250–500 ms intervals, respectively; these time windows were visually estimated from the across-participant grand-average ERPs and are typical for these components (Hillyard and Picton, 2011). Then each component was quantified as the mean activity within the time window defined by those points in the immediate leading and lagging edge of the P1/N1/P3 peak where the ERP amplitude was 75% of peak amplitude (Picton et al., 2000). To simplify analysis, each component was quantified at the scalp site(s) of maximal activity (O1 and O2 for the P1 component, CZ for the central N1 component, and POZ for the P3 component).

For graphical display, grand-average resting alpha reactivity spectra and PVT ERP waveforms were generated by averaging across participants for each condition and/or testing session. Alpha reactivity and ERP difference scalp topographies were visualized by computing between-condition differences for these responses at each electrode that were then displayed as interpolated topographical scalp maps using algorithms from the EEGLAB MATLAB toolbox.

2.6. Statistical analysis

Across-session differences in PVT RT, the three mood measures (PANAS, ERQ, CES-D),the four sleep measures (average daily sleep, circadian amplitude, circadian minimum, and rhythmicity of circadian activity rhythms), and the four electrophysiological measures (P1/central N1/P3 amplitude, alpha reactivity) were statistically assessed via generalized estimating equations (GEEs; Ghisletta and Spini, 2004; Gardiner et al., 2009). The GEE method is a modern generalized regression procedure that is better equipped to analyze longitudinal data than traditional statistical methods because they can account for missing and non-normally distributed data, estimate the correlation structure across repeated measure levels, and robustly estimate unbiased parameter standard errors (Ghisletta and Spini, 2004; Ma et al., 2012; White, 1980).

In the present study, the GEE analysis assumed a normal distribution with identity link, a robust covariance estimate, a maximum likelihood-estimate scale parameter, and an unstructured working correlation matrix (so that the correlational structure of the data across repeated measures was estimated from the data). In addition, the main analysis of average daily sleep across sessions and the cross-sectional regression relating average daily sleep to alpha reactivity also employed scale weights $\sim 1/\sigma_{response}$ in order

to correct for strong heteroscedasticity. GEEs were also used to perform cross-sectional regression analyses relating (1) average daily sleep, circadian rhythm measures, alpha reactivity and P1/P3 amplitude to PVT RT within sessions, and (2) average daily sleep and circadian rhythm measures to alpha reactivity and P1/P3 amplitude within sessions. Cross-sectional regression coefficients are reported in standardized units for ease of comparison among experimental variables. All reports of GEE analyses in this paper include tests of model effects (Wald χ^2 statistic values, associated degrees of freedom, p-values) and for post hoc tests, p-values of pairwise contrasts corrected for multiple comparisons via the Holm-Bonferroni procedure. All statistical analyses reported in this paper were performed using the SPSS software package (IBM Corporation, Armonk, NY, USA).

3. Results

3.1. Mood measures

There were no significant GEE model effects of testing session for the CES-D, ERQ, or positive affect component of the PANAS (ps < .11). However, the negative component of the PANAS significantly increased from Sessions 1 and 2 to Session 3; see Table 1. This indicates that the negative mood of the participants increased towards the end of the semester.

3.2. Average daily sleep and circadian activity rhythm

Average daily sleep significantly decreased from Session 1 to Sessions 2 and 3, but did not significantly differ between Sessions 2 and 3; see Table 1. This indicates that on average the college students in our sample were sleeping 6.7 h per night by the end of a semester, well below the recommended levels for optimal functioning (Bonnet and Arand, 1995; Centers for Disease Control and Prevention, 2013). In addition, the circadian minimum increased from Session 1 to Sessions 2 and 3, indicating an across-semester increase in nighttime activity and decrease in sleep quality; the circadian minimum did not significantly differ between Sessions 2 and 3; see Table 1. Furthermore, circadian activity became less rhythmic across the course of the semester, as indicated by significant decreases in the activity F-statistic from Session 1 to Session 3 and from Session 2 to Session 3; however, the F-statistic values did not significantly differ between Sessions 1 and 2; see Table 1. Finally, the test of GEE model effects for circadian amplitude was significant but there were only trend-level decreases from Session 1 to Sessions 2 and 3; see Table 1.

3.3. PVT performance

A significant test of GEE model effects indicated that PVT RT increased from Session 1 to Sessions 2 and 3; PVT RT did not significantly differ between Sessions 2 and 3; see Table 2. Furthermore, the cross-section regression analysis showed that average daily sleep was negatively associated with PVT RT within sessions, $\beta = -.26 \pm .1$, Wald $\chi^2_{1,24} = 8.15$, $p < .004$. That is, the more sleep a participant received around the time of testing (Session 1: the week after testing; Sessions 2 and 3: the week prior to testing), the faster their PVT RTs. The cross-section regression analysis revealed no significant relationships between PVT RT and the circadian rhythm measures Wald $\chi^2_{1,24} = 0.00–2.04$, ps < .459.

Finally, the test of GEE model effects for proportion of lapse trials was significant. Post-hoc testing indicated that the proportion of lapses increased from Session 1 to Session 2; however, the differences in lapses between these sessions and Session 3 were not significant, ps > .2; see Table 2.

3.4. Alpha reactivity

Fig. 2 shows the grand-averaged spectra of the resting EEG data at scalp site O2 for all three testing sessions. The spectra demonstrate a qualitative decrease in eyes closed alpha power and slight increase in eyes open alpha power from Session 1 to Sessions 2 and 3. These qualitative differences were captured by quantitative analysis of the AR index (see EEG Recording and Analysis for definition). A significant test of GEE model effects indicated that alpha reactivity decreased from Session 1 to Sessions 2 and 3, whereas alpha reactivity significantly increased from Session 2 to Session 3; see Table 2. In addition, the cross-section regression analysis showed alpha reactivity was negatively associated with PVT RT within sessions, $\beta = -0.21 \pm 0.09$, Wald $\chi^2_{1,24} = 5.71$, $p < .017$. Greater alpha reactivity was associated with faster PVT RTs within a testing session. Furthermore, average daily sleep was positively associated with alpha reactivity amplitude within sessions, $\beta = -0.2 \pm 0.09$, Wald $\chi^2_{1,24} = 4.70$, $p < .03$. That is, the more sleep a participant received around the time of testing, the greater their alpha reactivity at test. The rhythmicity of the circadian rhythm (F-statistic) was also positively associated with alpha reactivity amplitude within sessions, $\beta = 0.29 \pm 0.08$, Wald $\chi^2_{1,24} = 13.52$, $p < .001$; the more rhythmic (larger F value) a participant's circadian activity around time of testing, the greater their alpha reactivity at test.

Given that the PANAS negative scores of the participants increased towards the end of the semester (see Results – Mood Measures section, above), follow-up analyses were conducted with these scores included as an additional covariate. These follow-up analyses preserved the basic pattern of alpha reactivity effects described above except that the Session 1 vs. Session 3 post hoc alpha reactivity difference and the positive association between ADS and alpha reactivity were reduced to trend-level significance levels ($p < .075$ and $p < .06$, respectively). This suggests that a portion of the observed alpha reactivity changes (especially towards the end of the semester) is associated with changes in negative mood.

3.5. ERPs

The amplitudes of the P1 and central N1 ERP components did not significantly vary across sessions and were not significantly

Table 1
Mean PANAS –, sleep, and circadian activity measure values by session.

	PANAS –	Average daily sleep	Circadian minimum	Circadian F-statistic	Circadian amplitude
Session 1	16.13* (0.97)	423* (10)	2510* (204)	0.27* (0.05)	1.90* (0.05)
Session 2	17.92* (1.16)	396** (13)	2226** (212)	0.42* (0.06)	1.76* (0.07)
Session 3	20.67** (1.61)	403** (11)	1838** (163)	0.50** (0.07)	1.70* (0.07)
GEE analysis					
Wald $\chi^2_{2,24}$	10.48	11.85	10.40	11.68	6.62
$p <$	.005	.003	.006	.003	.037

Note: PANAS – and circadian measure values are dimensionless; average daily sleep units in minutes. SE values in parentheses. Measure values within a column and with different superscripts statistically differ in post hoc testing ($p < .05$).

Table 2
Mean PVT and electrophysiological measure values by session.

	PVT RT	PVT lapses	Alpha reactivity	P3 amplitude
Session 1	283* (6)	1.0* (0.4)	5.98* (0.54)	12.53* (0.91)
Session 2	299* (8)	5.0** (1.2)	3.20** (0.47)	9.77** (1.03)
Session 3	301** (9)	5.0** (2.2)	4.70** (0.57)	9.43** (0.95)
GEE analysis				
Wald $\chi^2_{2,24}$	8.01	14.26	32.61	23.41
$p <$	.018	.001	.001	.001

Note: PVT RT units in ms and lapses in %; alpha reactivity units in $\mu V^2/Hz$; P3 amplitude units in μV. SE values in parentheses. Numbers within a column and with different superscripts statistically differ in post hoc testing ($p < .05$).

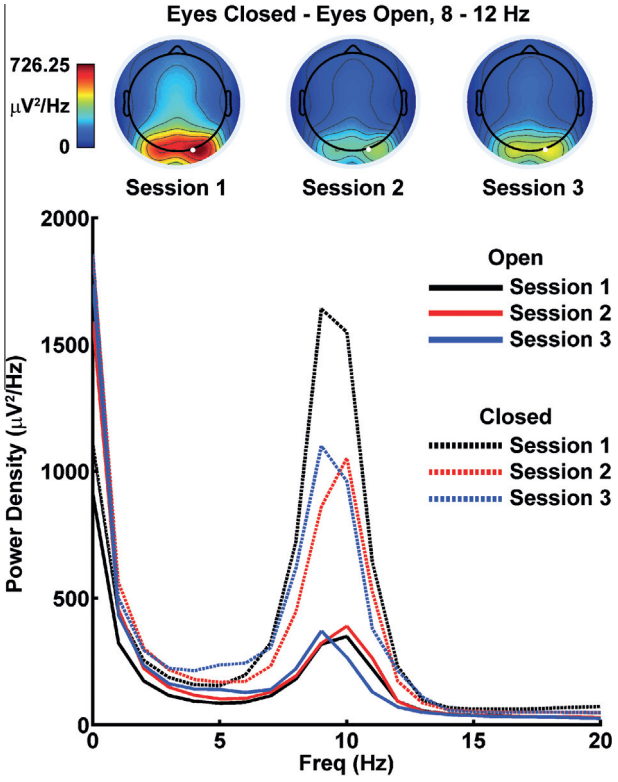

Fig. 2. Resting eyes closed (dashed lines) and eyes open (solid lines) EEG spectral power density at representative posterior scalp location O2 during testing Session 1 (black lines), Session 2 (red lines), and Session 3 (blue lines). Head maps show alpha reactivity (eyes open–eyes closed, 8–12 Hz) scalp topography for each session; blue to red colors indicate increasing alpha reactivity magnitude. White dot on scalp maps indicates O2 electrode location. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

related to PVT RT, average daily sleep, or any of the three circadian activity rhythm measures, *p*s > .177.

P3 ERP component amplitude decreased from Session 1 to Sessions 2 and 3 (see Fig. 3); see Table 2. P3 amplitude significantly decreased from Session 1 to Session 2 and Session 3, but P3 amplitude did not significantly differ between Sessions 2 and 3; see Table 2. In addition, the cross-section regression analysis showed P3 amplitude negatively predicted PVT RT within sessions, $\beta = -.27 \pm .14$, Wald $\chi^2_{1,24} = 3.99$, $p < .046$. Greater P3 amplitude was associated with faster PVT RTs within a testing session. However, ADS positively predicted P3 amplitude within sessions, $\beta = -.24 \pm .1$, Wald $\chi^2_{1,24} = 6.23$, $p < .012$. The more sleep a participant received around the time of testing, the greater their P3 amplitude during test. Follow-up analyses including PANAS negative mood component scores as an additional covariate did not change the

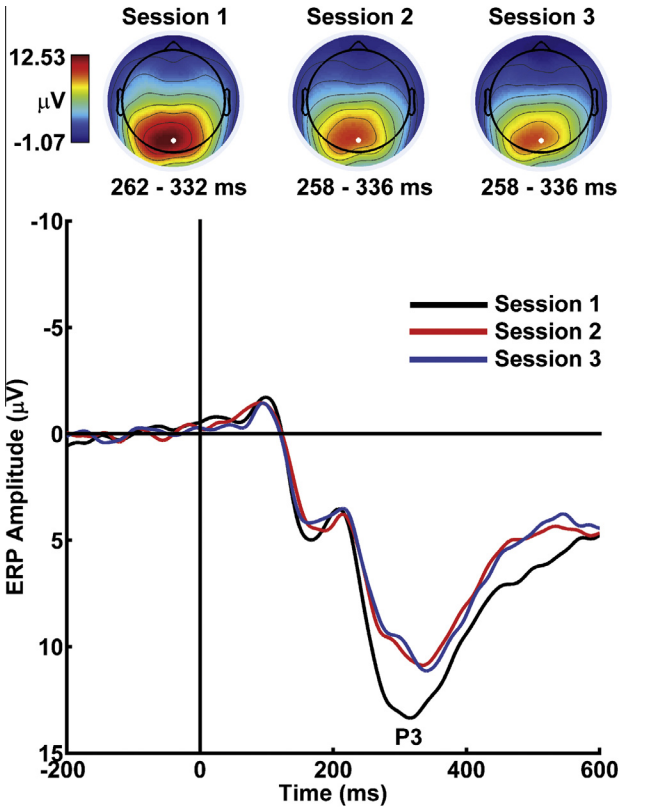

Fig. 3. Grand-average PVT timer-locked ERPs at representative site POZ during testing session 1 (black line), session 2 (red line), and session 3 (blue line). Head maps show P3 ERP scalp topography for each session. Red/blue colors indicate ± values; times indicate P3 quantification intervals. White dot on scalp maps indicates POZ electrode location. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

significance of the P3 findings; this indicates that changes in negative mood did not contribute to the P3 effects. P3 amplitude was not significantly related to any of the circadian activity rhythm measures, Wald $\chi^2_{1,24} = 0.01–0.44$, ps = 1.

4. Discussion

The present study investigated the neurocognitive correlates of changes in sleep patterns of college students across a complete semester – examining the relationship between sleep changes, cortical arousal and the ability to sustain attention. In general, the college student sample slept less over the course of a semester and showed a decreased ability to sustain attention during performance of the psychomotor vigilance task (PVT). The amount of sleep experienced by the participants throughout the academic semester negatively predicted mean PVT RT. These findings are consistent with the past literature of TSD and chronic sleep restriction effects on PVT performance that were conducted in a controlled environment (Lim and Dinges, 2008; Franzen et al., 2008; Hoedlmoser et al., 2011). However, previous studies have relied on the assumption that the PVT functions as an accurate gauge of vigilance in cases of sleep loss, an assumption rarely tested beyond the confines of the laboratory setting for such a long period of time (Belenky et al., 2003; Basner and Dinges, 2011). This study provides confirmatory evidence that the PVT is a valid and reliable measure for indexing changes in vigilance associated with sleep restriction over the course of 3 months.

In addition to the behavioral changes in vigilance, EEG-based measures of resting state cortical arousal (EEG alpha reactivity)

and vigilance (PVT counter-locked P3 ERP component) both decreased across early, mid, and late semester testing sessions. Furthermore, participant total sleep time positively predicted alpha reactivity level and P3 amplitude, both of which in turn negatively predicted PVT RT. This confirms the typical assumption that observed PVT performance decrements are related to a decrease in cortical arousal and/or vigilance resulting from sleep restriction. The present alpha reactivity patterns are consistent with previous work showing declines in alpha reactivity following sleep deprivation (Armington and Mitnick, 1959; Johnson et al., 1965; Lorenzo et al., 1995; Kornguth et al., 2013). Patients with Mild Cognitive Impairment and Alzheimer's disease similarly show a decrease in reactivity compared to healthy controls (Babiloni et al., 2010). Furthermore lack of alpha reactivity predicts poorer outcomes following brain injury (Zhang et al., 2011). These declines have been proposed to reflect lower thalamo-cortical functional connectivity (Babiloni et al., 2010). Previous research has shown that increased structural brain connectivity moderates the effects of sleep loss on cognition (Rocklage, Williams, Pacheco, & Schnyer, 2009). The present results suggest that changes in daily sleep patterns may also effect functional brain connectivity in ways that are currently not well understood. The present results suggest that changes in daily sleep patterns may also affect functional brain connectivity in ways that are currently not well understood. The present P3 ERP findings are consistent with previous research showing a general decrease in the amplitude of this component with sleep deprivation and sleep restriction (Humphrey et al., 1994; Harsh and Badia, 1989; Trujillo et al., 2009). Although the amplitude of the P3 component is known to vary as a function of stimulus probability, stimulus meaning, and the amount of information transmitted by a stimulus (Johnson Jr., 1985), the present P3 findings suggest an influence of sleep restriction on processing related to stimulus meaning and/or transmitted information because stimulus probability was not manipulated in the PVT. Nevertheless, it is possible that the present results may be more robust using an oddball paradigm that manipulates stimulus probability. Further research is needed to determine the relative impact of sleep deprivation on these processes.

It should be noted that no P1 or central N1 changes related to sleep loss were observed in the present study. This is in contrast to the studies of Hoedlmoser et al. (2011) and Trujillo et al., which respectively observed sleep deprivation-related changes in the early P1 and central N1 ERP components. It is possible that large amounts of sleep loss (larger than observed in the present study) are necessary before the low-level automatic neurocognitive processes reflected by these ERP components are negatively affected. More research is needed to test this hypothesis.

In addition to the measure of average daily sleep, circadian measures were also computed. Circadian minimum, which represents nighttime activity or disturbance, increased across the semester. There was also a decrease in both the F statistic and circadian amplitude, which represent the robustness of the circadian cycle and the strength of the sleep-wake cycle respectively. These additional measures, independent of average daily sleep, primarily demonstrate that changes in cortical arousal correlated with changes in sleep-wake patterns. For example in this experiment, the decrease in the F statistic value was correlated with a decrease in the alpha reactivity which previous research has identified as linked to general cortical arousal (Kornguth et al., 2013). Interestingly, an increase in the F statistic value has been linked with dementia and thus further supports the argument that it reflects cortical arousal (Tranah et al., 2011). Unlike average daily sleep, which captures both cortical and cognitive functioning, circadian measures identify cortical arousal and thereby appear to display another aspect of neurological changes caused by altered sleep.

In the present study, most of the significant observational differences occurred between Session 1 and Sessions 2 and 3 (the exception to this was a small alpha reactivity increase from Session 2 to Session 3). Is it possible that, rather than sleep restriction, these effects reflect the novelty of the data collection experience in Session 1? This possibility seems unlikely for three reasons. First, the PVT has minor learning effects over repeated assessments (Lim and Dinges, 2008), whereas in more complex tasks RTs typically decrease with task repetition (e.g., Johnson et al., 2005) rather than increase as was observed here. Second, regression analyses showed significant relationships between the amount of sleep in the 1-week period assessed for each testing session and both PVT RT and the electrophysiological measures. Given that these regression analyses were cross-sectional in that they indexed individual participant variation *collapsed across session*, they cannot reflect a between-session change in novelty. A more probable explanation for the present pattern of across-session differences lies in the amount of inter-subject variability in sleep from session to session. Some subjects continuously declined in sleep amount/quality across the semester whereas others showed upright or inverted u-shaped sleep changes; this state of affairs yielded only a 30 min decrease in sleep on average across the semester. Thus the small effects in sleep and performance observed in the group averages likely reflect the fact that most participants suffered a substantial change in sleep from the beginning to the middle portion of the semester, after which sleep loss was either maintained until the semester end or increased/decreased in different subgroups of subjects such that there was no change in the overall group-average from the middle to the end of the semester.

One limitation of the present study is that sleep patterns were assessed with actigraphy rather than polysomnography (PSG), which is considered gold standard in sleep research. However, the use of PSG in a longitudinal field study is highly impractical and actigraphy remains a moderately valid and reliable technique to assess sleep-wake patterns in normal, healthy adult populations (Ancoli-Israel et al., 2003; Marino et al., 2013). A second limitation of the present study is that the sleep-wake patterns of college students may not be representative of the general population as a whole. In order to reduce this difference, we chose students who had stable academic performance. Additionally, it is unlikely that the neurocognitive changes observed in the present study were solely due to the stress of the school semester because the behavior and EEG-based measures showed a significant predictive relationship to sleep. Finally a third limitation of the present study was that it was exploratory in nature and thus did not use control and experimental groups. It would be beneficial to record from an extended duration to examine how long it takes for PVT reaction time performance to return to baseline after total sleep time returns to levels seen at the beginning of the study.

5. Conclusion

The present study has provided evidence that changes in total sleep time and circadian rhythm have a demonstrable effect on cortical reactivity and the maintenance of vigilance. These findings are important because they demonstrate the critical nature of sleep for optimizing neurocognitive performance and show that long-term shifts in sleep patterns, both total time spent asleep and the quality of that sleep measured through circadian rhythm, have significant effects.

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The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Appendix A.

In the analysis presented in the main article, average daily sleep and circadian rhythm activity measures (amplitude, minimum, F-statistic) were calculated using data acquired over the week directly following testing Session 1, whereas sleep measures for Sessions 2 and 3 were calculated using data acquired over the week prior to each of these testing sessions (see Methods: Actigraphic Recording and Data Reduction section of the main article). This choice was made because (1) actigraph data prior to Session 1 were only available for nine of the 24 participants and (2) it was assumed that average daily sleep and circadian activity should have remained fairly stable across the weeks immediately before and after each testing session. This latter assumption was justified by a group analysis comparing the sleep measures before and after Session 1 for those nine participants with pre-Session 1 actigraph data, as well as before and after Session 2 for all 24 participants (a pre/post analysis was not performed for the third session, as no post-Session 3 actigraph data were available).

Average daily sleep across the weeks immediately prior to Session 1 and Session 2 did not significantly differ from average daily sleep across the weeks immediately following each session (Session 1; 424 ± 11 min vs. 422 ± 13 min, Wald χ^2 (1, $N = 9$) = 0.03, $p < .87$; Session 2; 399 ± 13 min vs. 412 ± 14 min, Wald χ^2 (1, $N = 24$) = 1.27, $p < .26$). In addition, average daily sleep demonstrated a significant positive relationship between the weeks immediately before and after each testing session (Session 1: $\beta = 0.32 \pm 0.16$, Wald χ^2 (1, $N = 9$) = 3.74, $p < .053$; Session 2: $\beta = 0.75 \pm 0.10$, Wald χ^2 (1, $N = 24$) = 56.45, $p < .001$). These findings suggest that the average daily sleep patterns before and after each testing sessions were similar.

The three circadian rhythm activity measures calculated for the weeks immediately prior to Session 1 and Session 2 also did not significantly differ from these measures computed for the week immediately following each session (Session 1 amplitude: 2.02 ± 0.04 vs. 2.02 ± 0.06, Wald χ^2 (1, $N = 9$) = 0.002, $p < .966$; Session 1 minimum: 0.20 ± 0.04 vs. 0.21 ± 0.06, Wald χ^2 (1, $N = 9$) = 0.003, $p < .960$; Session 1 F-statistic: 2746.23 ± 282.72 vs. 2865.00 ± 331.83, Wald χ^2 (1, $N = 9$) = 0.136, $p < .712$; Session 2 amplitude: 1.76 ± 0.07 vs. 1.74 ± 0.06, Wald χ^2 (1, $N = 24$) = 0.06, $p < .814$; Session 2 minimum: 0.42 ± 0.06 vs. 0.43 ± 0.06, Wald χ^2 (1, $N = 24$) = 0.18, $p < .674$; Session 2 F-statistic: 2226.30 ± 212.21 vs. 2338.96 ± 238.11, Wald χ^2 (1, $N = 24$) = 0.44, $p < .509$). Furthermore, the circadian rhythm activity measures also demonstrated positive relationships between the weeks immediately before and after each testing session. For the pre- and post-Session 1 comparisons, this relationship was significant for the F-statistic measure ($\beta = 0.46 \pm 0.15$, Wald χ^2 (1, $N = 9$) = 9.77, $p < .002$), but not the other two measures (amplitude: $\beta = 0.28 \pm 0.24$, Wald χ^2 (1, $N = 9$) = 1.27, $p < .260$; minimum: $\beta = 0.15 \pm 0.31$, Wald χ^2 (1, $N = 9$) = 0.238, $p < .626$). However, the positive relationships between the pre- and post-Session 2 circadian rhythm activity measures were all significant (amplitude: $\beta = 0.74 \pm 0.14$, Wald χ^2 (1, $N = 24$) = 29.34, $p < .001$; minimum: $\beta = 0.79 \pm 0.08$, Wald χ^2 (1, $N = 24$) = 112.01, $p < .001$; F-statistic: $\beta = 0.72 \pm 0.14$, Wald χ^2 (1, $N = 24$) = 27.59, $p < .001$). These findings suggest that the patterns of circadian rhythm activity before and after each testing session were also similar.

References

Ancoli-Israel S, Martin JL, Kripke DF, Marler MR, Klauber MR. Effect of light treatment on sleep and circadian rhythms in demented nursing home patients. J Am Geriatr Soc 2002;50:282–9.

Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. Sleep 2003;26:342–92.

Armington JC, Mitnick LL. Electroencephalogram and sleep deprivation. J Appl Physiol 1959;14:247–50.

Babiloni C, Lizio R, Vecchio F, Frisoni GB, Pievani M, Geroldi C, et al. Reactivity of cortical alpha rhythms to eye opening in mild cognitive impairment and Alzheimer's disease: an EEG study. J Alzheimers Dis 2010;22:1047–64.

Balkin TJ, Bliese PD, Belenky G, Sing H, Thorne DR, Thomas M, et al. Comparative utility of instruments for monitoring sleepiness-related performance decrements in the operational environment. J Sleep Res 2004;13:219–27.

Basner M, Dinges DF. Maximizing sensitivity of the psychomotor vigilance test (PVT) to sleep loss. Sleep 2011;34:581.

Belenky G, Wesensten NJ, Thorne DR, et al. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose–response study. J Sleep Res 2003;12:1–12.

Bonnet MH, Arand DL. We are chronically sleep deprived. Sleep 1995;18:908–11.

Buboltz Jr WC, Brown F, Soper B. Sleep habits and patterns of college students: a preliminary study. J Am Coll Health 2001;50:131–5.

Carpenter S. Sleep deprivation may be undermining teen health. Monit Psychol 2001;32:32.

Center for Disease Control and Prevention [Insufficient Sleep is a Public Health Epidemic], <http://www.cdc.gov/features/dssleep/index.html>; March 14, 2013 (accessed 5.01.2014).

Cole R, Kripke D, Gruen W, Mullaney D, Gillin J. Automatic sleep/wake identification from wrist activity. Sleep 1992;15:461–9.

Coren S. The prevalence of self-reported sleep disturbances in young adults. Int J Neurosci 1994;79:67–73.

Crawford JR, Henry JD. The Positive and Negative Affect Schedule (PANAS): construct validity, measurement properties and normative data in a large non-clinical sample. Brit J Clin Psychol 2004;43:245–65.

Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J Neurosci Methods 2004;134:9–21.

Dinges DF, Powell JW. Microcomputer analyses of performance on portable, simple visual RT task during sustained operations. Behav Res Methods Instr 1985;17:652–5.

Dinges DF, Pack F, Williams K, Gillen KA, Powell JW, Ott GE, et al. Cumulative sleepiness, mood disturbance and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 h per night. Sleep 1997;20:267–77.

Doran SM, Van Dongen HPA, Dinges DF. Sustained attention performance during sleep deprivation: evidence of state instability. Arch Ital Biol 2001;139:253–67.

Drake CL, Roehrs TA, Burduvali E, Bonahoom A, Rosekind M, Roth T. Effects of rapid versus slow accumulation of eight hours of sleep loss. Psychophysiology 2001;38:979–87.

Fabre-Thorpe M, Delorme A, Marlot C, Thorpe S. A limit to the speed of processing in ultra-rapid visual categorization of novel scenes. J Cogn Neurosci 2001;13:171–80.

Fallone G, Acebo C, Arnedt JT, Seifer R, Carskadon MA. Effects of acute sleep restriction on behavior, sustained attention, and response inhibition in children. Percept Mot Skills 2001;93:213–29.

Franzen PL, Siegle GJ, Buysse DJ. Relationships between affect, vigilance, and sleepiness following sleep deprivation. J Sleep Res 2008;17:34–41.

Gardiner JC, Luo Z, Roman LA. Fixed effects, random effects and GEE: What are the differences? Stat Med 2009;28:221–39.

Ghisletta P, Spini D. An introduction to generalized estimating equations and an application to assess selectivity effects in a longitudinal study on very old individuals. J Educ Behav Stat 2004;29:421–37.

Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.

Harrison Y, Horne JA. The impact of sleep deprivation on decision making: a review. J Exp Psychol Appl 2000;6:236–49.

Harsh J, Badia P. Auditory evoked potentials as a function of sleep deprivation. Work Stress 1989;3:79–91.

He P, Wilson G, Russell C. Removal of ocular artifacts from electro-encephalogram by adaptive filtering. Med Biol Eng Comput 2004;42:407–12.

Hillyard SA, Picton TW. Electrophysiology of cognition. Compr Physiol 2011:519–84.

Hoedlmoser K, Griessenberger H, Fellinger R, Freunberger R, Klimesch W, Gruber W, et al. Event-related activity and phase locking during a psychomotor vigilance task over the course of sleep deprivation. J Sleep Res 2011;20:377–85.

Humphrey DG, Kramer AF, Stanny RR. Influence of extended wakefulness on automatic and nonautomatic processing. Hum Factors 1994;36:652–69.

Jean-Louis G, Kripke DF, Mason WJ, Elliott JA, Youngstedt SD. Sleep estimation from wrist movement quantified by different actigraphic modalities. J Neurosci Methods 2001;105:185–91.
Johnson LC, Slye ES, Dement W. Electroencephalographic and autonomic activity during and after prolonged sleep deprivation. Psychosom Med 1965;27:415–23.
Johnson Jr R, Barnhardt J, Zhu J. Differential effects of practice on the executive processes used for truthful and deceptive responses: an event-related brain potential study. Cogn Brain Res 2005;24:386–404.
Johnson Jr R. A triarchic model of P300 amplitude. Psychophysiology 1985;23:367–84.
Jugovac D, Cavallero C. Twenty-four hours of total sleep deprivation selectively impairs attentional networks. J Expl Psychol 2012;59:115–23.
Jung CM, Ronda JM, Czeisler CA. Comparison of sustained attention assessed by auditory and visual psychomotor vigilance tasks prior to and during sleep deprivation. J Sleep Res 2011;20:348–55.
Kong D, Soon CS, Chee MW. Functional imaging correlates of impaired distractor suppression following sleep deprivation. Neuroimage 2012;61:50–5.
Kornguth S, Steinberg R, Schnyer D, Trujillo L. Integrating the human into the total system: degradation of performance under stress. Nav Eng J 2013;125:85–90.
Lack LC. Delayed sleep and sleep loss in university students. J Am Coll Health 1986;35:105–10.
Lim J, Dinges DF. Sleep deprivation and vigilant attention. Ann NY Acad Sci 2008;1129:305–22.
Littner M, Kushida CA, Anderson WM, Bailey D, Berry RB, Davila DG, et al. Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: an update for 2002. Sleep 2003;26:337–41.
Lorenzo I, Ramos J, Arce C, Guevara MA. Effect of total sleep deprivation on reaction time and waking EEG activity in man. Sleep 1995;18:346–54.
Ma Y, Mazumdar M, Memtsoudis SG. Beyond repeated measures ANOVA: advanced statistical methods for the analysis of longitudinal data in anesthesia research. Reg Anesth Pain Med 2012;37:99–105.
Maddox WT, Glass BD, Zeithamova D, Savarie ZR, Bowen C, Matthews MD, et al. The effects of sleep deprivation on dissociable prototype learning systems. Sleep 2011;34:253–60.
Marino M, Li Y, Rueschman MN, Winkelman JW. Measuring sleep: accuracy, sensitivity, and specificity of wrist actigraphy compared to polysomnography. Sleep 2013;36:1747–55.
Marler MR, Gehrman P, Martin JL, Ancoli-Israel S. The sigmoidally transformed cosine curve: a mathematical model for circadian rhythms with symmetric non-sinusoidal shapes. Stat Med 2006;25:3893–904.
Martin J, Marler MR, Shochat T, Ancoli-Israel S. Circadian rhythms of agitation in institutionalized patients with Alzheimer's disease. Chronobiol Int 2000;17:405–18.
Niedermeyer E. The normal EEG of the waking adult. In: Niedermeyer E, Lopes Da Silva F, editors. Electroencephalography: Basic Principles, Clinical Applications and Related Fields. 4th ed. Baltimore, MD: Williams and Wilkens; 1999. p. 149–73.
Perrin F, Perrier J, Bertrand O, Giard MH, Echallier JF. Mapping of scalp potentials by surface spline interpolation. Electroen Clin Neuro 1987;66:75–81.
Picton TW, Bentin S, Berg P, Donchin E, Hillyard SA, Johnson Jr R, et al. Guidelines for using human event-related potentials to study cognition: recording standards and publication criteria. Psychophysiology 2000;37:127–52.
Pollak CP, Tryon WW, Nagaraja H, Dzwonczyk R. How accurately does wrist actigraphy identify the states of sleep and wakefulness? Sleep 2001;24:957–65.
Savard J, Liu L, Natarajan L, et al. Breast cancer patients have progressively impaired sleep–wake activity rhythms during chemotherapy. Sleep 2009;32:1155.
Smith ME, McEvoy LK, Gevins A. The impact of moderate sleep loss on neurophysiologic signals during working-memory task performance. Sleep 2002;25:56–66.
Rocklage M, Williams V, Pacheco J, Schnyer DM. White matter differences predict cognitive vulnerability to sleep deprivation. Sleep 2009;32:1100–3.
Taras H, Potts-Datema W. Sleep and student performance at school. J Sch Health 2005;75:248–54.
Tranah GJ, Blackwell T, Stone KL, et al. Circadian activity rhythms and risk of incident dementia and mild cognitive impairment in older women. Ann Neurol 2011;70:722–32.
Trujillo LT, Kornguth S, Schnyer DM. An ERP examination of the differential effects of sleep deprivation on exogenously cued and endogenously cued attention. Sleep 2009;32:1285–97.
Tucker AM, Whitney P, Belenky G, Hinson JM, Van Dongen HP. Effects of sleep deprivation on dissociated components of executive functioning. Sleep 2010;33:47–57.
Vanderlind MW, Beevers CG, Sherman SM, Trujillo LT, McGeary JE, Matthews, et al. Sleep and sadness: exploring the relation among sleep, cognitive control, and depressive symptoms in young adults. Sleep Med 2014;15:144–9.
Vgontzas AN, Zoumakis E, Bixler EO, et al. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. J Clin Endocr Metab 2004;89:2119–26.
Warm JS, Parasuraman R, Matthews G. Vigilance requires hard mental work and is stressful. Hum Factors 2008;50:433–41.
White HA. Heteroskedasticity-consistent covariance matrix estimator and a direct test for heteroskedasticity. Econometrica 1980;48:817–38.
Zhang Y, Su YY, Haupt WF, Zhao JW, Xiao SY, Li HL, et al. Application of electrophysiologic techniques in poor outcome prediction among patients with severe focal and diffuse ischemic brain injury. J Clin Neurophysiol 2011;28:497–503.