Human Performance Deterioration Due to Prolonged Wakefulness Can Be Accurately Detected Using Time-Varying Spectral Analysis of Electrodermal Activity

Hugo F. Posada-Quintero, and **Jeffrey B. Bolkhovsky**, University of Connecticut, Storrs, **Michael Qin**, Naval Submarine Medical Research Laboratory, New London, CT, and **Ki H. Chon**, University of Connecticut, Storrs

Objective: The aim was to determine if indices of the autonomic nervous system (ANS), derived from the electrodermal activity (EDA) and electrocardiogram (ECG), could be used to detect deterioration in human cognitive performance on healthy participants during 24-hour sleep deprivation.

Background: The ANS is highly sensitive to sleep deprivation.

Methods: Twenty-five participants performed a desktop-computer-based version of the psychomotor vigilance task (PVT) every 2 hours. Simultaneously with reaction time (RT) and false starts from PVT, we measured EDA and ECG. We derived heart rate variability (HRV) measures from ECG recordings to assess dynamics of the ANS. Based on RT values, average reaction time (avRT), minor lapses (RT > 500 ms), and major lapses (RT > 1 s) were computed as indices of performance, along with the total number of false starts.

Results: Performance measurement results were consistent with the literature. The skin conductance level, the power spectral index, and the high-frequency components of HRV were not significantly correlated to the indices of performance. The nonspecific skin conductance responses, the time-varying index of EDA (TVSymp), and normalized low-frequency components of HRV were significantly correlated to indices of performance ($p < 0.05$). TVSymp exhibited the highest correlation to avRT (–0.92), major lapses (–0.85), and minor lapses (–0.83).

Conclusion: We conclude that indices that account for high-frequency dynamics in the EDA, specifically the time-varying approach, constitute a valuable tool for understanding the changes in the autonomic nervous system.

Application: This can be used to detect the adverse effects of prolonged wakefulness on human performance.

Keywords: electrodermal activity, heart rate variability, autonomic nervous system, prolonged wakefulness, performance

Address correspondence to Hugo F. Posada-Quintero, Department of Biomedical Engineering, University of Connecticut, Engineering and Science Building, Room 407, Storrs, CT 06269-3247, USA; e-mail: h.posada@engr.uconn.edu.

HUMAN FACTORS
Vol. XX, No. X, Month XXXX, pp. 1–13
DOI: 10.1177/0018720818781196

INTRODUCTION

This work presents the results of correlation analysis between indices of performance on the psychomotor vigilance task (PVT) and noninvasive measures of the autonomic nervous system (ANS) based on heart rate variability (HRV) and electrodermal activity (EDA), during a 24-hour period of sleep deprivation. We recently conducted a study looking at the effects of prolonged wakefulness on participants performing the error awareness task (EAT) (Posada-Quintero, Bolkhovsky, Reljin, & Chon, 2017). We observed that high frequency (HF) dynamics of EDA known as the skin conductance responses (SCRs) were more sensitively correlated to sleep deprivation than were the slow dynamics, defined as the skin conductance level (SCL). However, we could not directly compare with other studies looking at performance deterioration as a byproduct of prolonged wakefulness, because most studies measured participants' response to the PVT, not the EAT (Posada-Quintero et al., 2017). The PVT, which measures a person's reaction time (RT) to the presentation of concurrent stimuli, is a widely used standard for studying the effects of prolonged wakefulness, mainly because it has a proven strong correlation with both lack of sleep as well as with the circadian rhythm (Lim & Dinges, 2008). PVT allows us to observe the lapses or short periods of nonaction produced by deterioration of vigilant attention and has been proven to work as an indirect measure of sleep deprivation (Dinges, 1995).

Early detection is valuable for mitigating the consequences of performance deterioration due to the effects that sleep deprivation produces on human physiology. Human performance deterioration causes accidents in jobs that frequently

require working long hours, repetitive tasks, or late-night shifts (Costa, 1996), resulting in a large social and economic cost (Leger, 1994; Lyznicki, Doege, Davis, & Williams, 1998). Sleep deprivation also causes a marked effect on the ANS (Liu, Verhulst, Massar, & Chee, 2015; Michail, Kokonozi, Chouvarda, & Maglaveras, 2008; Zhong et al., 2005). In response to stressors of any kind, the ANS compensates by altering the balance between the parasympathetic and the sympathetic nervous systems. A predominantly parasympathetic tone is not an appropriate response to the fatigue stressor as it should elicit sympathetic activity instead, indicating a progression toward a state of decompensation and failure of physiological functions (Baharav et al., 1995; Cooke et al., 2006; Furman, Baharav, Cahan, & Akselrod, 2008; Michail et al., 2008; Winchell & Hoyt, 1997). Alternatively, the body benefits from a predominantly sympathetic response to fatigue (Appenzeller, 1987). The ANS is a preferred target for the development of an objective physiological measure of the effects of prolonged wakefulness, because of its high sensitivity to sleep deprivation (Fullagar et al., 2015; Izawa, Sugaya, Yamamoto, Ogawa, & Nomura, 2010; Koss & Davison, 1976; Tobaldini et al., 2013).

HRV is a noninvasive tool that allows for quantitative assessment of the ANS dynamics (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). In the frequency domain, the low-frequency (LF) components (0.045 to 0.15 Hz) of HRV are influenced by both the sympathetic and parasympathetic functions; the HF components (0.15 to 0.4 Hz) are only influenced by the parasympathetic nervous system (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Spectral indices of HRV have been used to assess the dynamics of the ANS, and it was suggested that the markers of parasympathetic and sympathetic activities are largely found in the HFs and LFs, respectively (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). The effects of sleep deprivation on HRV have been extensively studied, with different levels of success (Chua et al., 2012; Fogt, Cooke, Kalns, & Michael, 2011; Fogt, Kalns, & Michael, 2010; Glos, Fietze, Blau, Baumann, & Penzel, 2014; Nakano et al., 2000; Pagani et al., 2009; Vicente, Laguna, Bartra, & Bailón, 2016; Viola, James, Archer, & Dijk, 2008; Zhong et al., 2005). In general, these studies found that HRV alone has a limited potential to delineate the effects of sleep deprivation.

EDA measures the changes in electrical conductance of the skin. EDA is highly correlated to sweat production and is considered a pure assay of sympathetic activity because there is no parasympathetic innervation of eccrine sweat glands (Dawson, Schell, & Filion, 2007). As a result, EDA has gained popularity as a possible noninvasive tool for the separate assessment of the skin sympathetic activities (Boucsein, 2012; Colbert, Spaulding, Larsen, Ahn, & Cutro, 2011; Freeman & Chapleau, 2013). Traditional analysis of EDA signals is performed in the time domain, consisting of evaluation of the SCLs and SCRs (Boucsein et al., 2012). The LF dynamics of the EDA signal are exhibited in the SCL and the rapid phase fluctuations are demonstrated in the SCRs. Furthermore, indices based on spectral analyses of EDA (time-invariant and time-variant) have been recently reported as good surrogate measures of sympathetic dynamics (Posada-Quintero, Florian, Orjuela-Cañón, & Chon, 2016; Posada-Quintero, Florian, Orjuela-Cañón, Aljama-Corrales, et al., 2016). The combination of time and frequency information derived from the analysis of EDA improved the consistency and sensitivity of the technique (Posada-Quintero, Florian, Orjuela-Cañón, & Chon, 2016) when compared to using either only the time or frequency features.

Recent literature emphasizes the importance of EDA for the assessment of sympathetic function to better understand the altered reactions of sleep-deprived people (Liu et al., 2015; Miró, Cano-Lozano, & Buela-Casal, 2002). However, those studies did not explore the occurrence of rapid shifts (usual in the EDA signal) but focused only on the changes in SCL (low components of the signal). In a previous study, we found significant changes in the higher frequency components of EDA after 18 hours of sleep deprivation (Posada-Quintero et al., 2017). Hence, we

expect that changes in the higher frequencies of the EDA signal correlate with the observed deterioration of participant performance resulting from prolonged wakefulness. To evaluate this conjecture, we measured psychomotor vigilance with a commonly run test used as a measure of performance in humans during a 24-hour sleep deprivation period and concurrently collected HRV and EDA data.

MATERIALS AND METHODS

Participants

For this study, 25 healthy volunteers (14 males and 11 females; ages ranging from 18 to 45) were recruited. The sample size was chosen to be large enough for detecting differences in performance and for determining correlation. A sample size of 25 is sufficient to be able to detect differences in the PVT measures with a power higher than 0.95 based on the variance of previous studies that have reported on similar metrics (Chua et al., 2012; Dorrian, Rogers, & Dinges, 2005). Furthermore, this sample size allows us to detect a correlation higher than 0.75 with a power of 0.9 (Zar, 1999).

We kept the participants awake for at least 24 hours, with constant experimenter observation throughout the experiment to ensure the validity of the study. Seven days prior to the experiment, we gave the participants a data sheet to record their sleep schedule for the 7 days, to indicate compliance to the experimental constraints and expose potential outliers. Participants were compensated for their time but were not compensated for their level of performance. The study protocol was approved by the University of Connecticut Institutional Review Board in compliance with all applicable federal regulations governing the protection of human participants. All participants gave written informed consent in accordance with the Declaration of Helsinki.

Protocol

We instructed the participants to avoid all ingestion of stimulants and depressants 48 hours prior to the start of the experiment. We provided food during the experiment, to make sure the participants followed the dietary constraints of this study. Participants were required to be present at the experimental facility, located at the University of Connecticut, no more than 2 hours after waking up on the morning they started the experiment. Each participant performed a PVT trial every other hour (for a total of 12 trials, with Trial 12 occurring after 25 hours of sleep deprivation) during the 24-hour period. To complete all trials, participants remained in the facility for more than 25 hours. The first trial was used for training purposes and took place during the first hour after arrival.

A GSR amplifier FE116 (fully isolated AC excitation and automatic zeroing low voltage amplifier, 22 mVrms at 75 Hz, ADINSTRUMENTS) was used to collect EDA data, and an HP 78354A ECG monitor (Hewlett-Packard, FDA approved) was used to collect ECG data. The level of the EDA device was adjusted to zero at the start of every trial for calibration purposes. Five minutes prior to each task trial starting, we placed the electrodes to collect EDA data (stainless steel) on the middle and index fingers of each participant's nondominant hand. For recording ECG data, three hydrogel Ag/AgCl electrodes were placed on the participant's chest. During every trial, ECG and EDA data were simultaneously recorded. No filtering was applied to the data during the recording.

The PVT measures speed of reaction to visual stimuli over a period of time, for the purpose of assessing sustained attention. Participants used an application on a desktop computer (Khitrov et al., 2014) to perform the task for 10-minute trials throughout the course of their study. The same computer was used for all participants. During the 10-minute period, participants were presented with stimuli, in the form of numbers appearing on the screen. Participants were asked to click the mouse as fast as possible whenever they saw a number appear. The interstimuli interval was randomly determined and initiated within 2 to 10 seconds. For all the stimuli presented during the 10-minute period, RT was computed between the appearance of the numbers and left button click on the mouse, as well as false starts (responses with no stimuli).

Physiological Indices of the ANS

Data acquired while the participants were performing the PVT were used to compute

noninvasive measures of the ANS based on EDA and spectral analysis of HRV. To procure quality of physiological data, participants were asked to keep torso (where ECG electrodes were placed) and nondominant hand (where EDA was collected) still while performing the trials.

Indices of EDA. Time- and frequency-domains analysis was used to compute indices of EDA. In the time domain, the EDA signal was decomposed into tonic and phasic components, using the convex optimization approach (Greco, Valenza, Lanata, Scilingo, & Citi, 2016). The SCL (expressed in microsiemens, μS), an index related to the slow shifts of EDA, was computed as the mean value of the tonic component of EDA taken during a 2-minute period (Boucsein et al., 2012). The SCRs are the rapid transient events contained in the phasic component of the EDA signal. Given that the stimuli presented to the participants were all identical (click the mouse as fast as possible whenever they saw a number appear) and repeated multiple times, characterization of individual SCRs is not appropriate. The frequency of nonspecific SCRs (NSSCRs) was measured as the number of SCRs whose amplitude is higher than a given threshold (0.05 μS, in this study), per minute (Boucsein et al., 2012). NSSCRs were extracted automatically utilizing the convex optimization approach (Greco et al., 2016). In this study, for each trial, the first 2 minutes of EDA data were extracted while the participant was performing the PVT, to compute SCL and NSSCRs. Figure 1 shows EDA and HRV data collected during baseline and PVT task stages, for a given participant and trial. Notice the increase of SCL and SCR amplitudes and frequencies during PVT.

The power spectral measures were computed using the same 2 minutes of EDA data used to compute time-domain measures. Welch's periodogram method with 50% data overlap was used to calculate the time-invariant spectra of the EDA. A 128-datapoint length Blackman window was applied to each segment, the power spectrum of each windowed segment was computed using the fast Fourier transform, and the average of the power spectra was computed. The power in the range from 0.045 to 0.25 Hz was integrated to compute the time-invariant spectral index of EDA (EDASymp [μS2]). EDASymp was previously found to be sensitive to cognitive stress (Posada-Quintero, Florian, Orjuela-Cañón, Aljama-Corrales, et al., 2016).

For the time-varying analysis, we used variable frequency complex demodulation (VFCDM). VFCDM provides accurate amplitude estimates and one of the highest time-frequency resolutions (Chon, Dash, & Ju, 2009). As defined in a previous study, the VFCDM time-frequency representation of EDA was used to obtain the time-varying index of EDA (TVSymp). The TVSymp is calculated using the components that account for the power in the 0.08 to 0.24 Hz range (Posada-Quintero, Florian, Orjuela-Cañón, & Chon, 2016).

Indices of HRV. To compute HRV indices, 4 minutes of clean ECG segments were extracted from the data while the participant performed the PVT trials. The noise and motion artifacts of the ECG data were reduced using a band-pass filter (0.05–40 Hz). For HRV analysis, the R peaks were detected using a publicly available algorithm (Nygaards & Sörnmo, 1983; Vidaurre, Sander, & Schlögl, 2011). R peaks were manually corrected to ensure that all beats were correctly detected. Subsequently, the RR interval series for each trial were computed. The RR interval series were converted to an evenly time-sampled signal (4 Hz) by cubic spline interpolation. The Welch's periodogram with 50% data overlap was used to compute the power spectra of HRV. A 256-point Blackman window was applied to the segments. The power spectra were calculated for each windowed segment, and the average of the power spectra was computed.

The LF (HRVLF [ms2]) and the HF index (HRVHF [ms2]) were computed by integrating the frequency ranges of 0.045 to 0.15 Hz and 0.15 to 0.4 Hz, respectively. Normalized versions of these two (HRVLFn and HRVHFn, in normalized units [n.u.]) were computed by dividing the indices by the total power of HRV (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). HRVLF and HRVLFn are used as indices of sympathetic tone. Likewise, HRVHF and HRVHFn are used as indices of parasympathetic control.

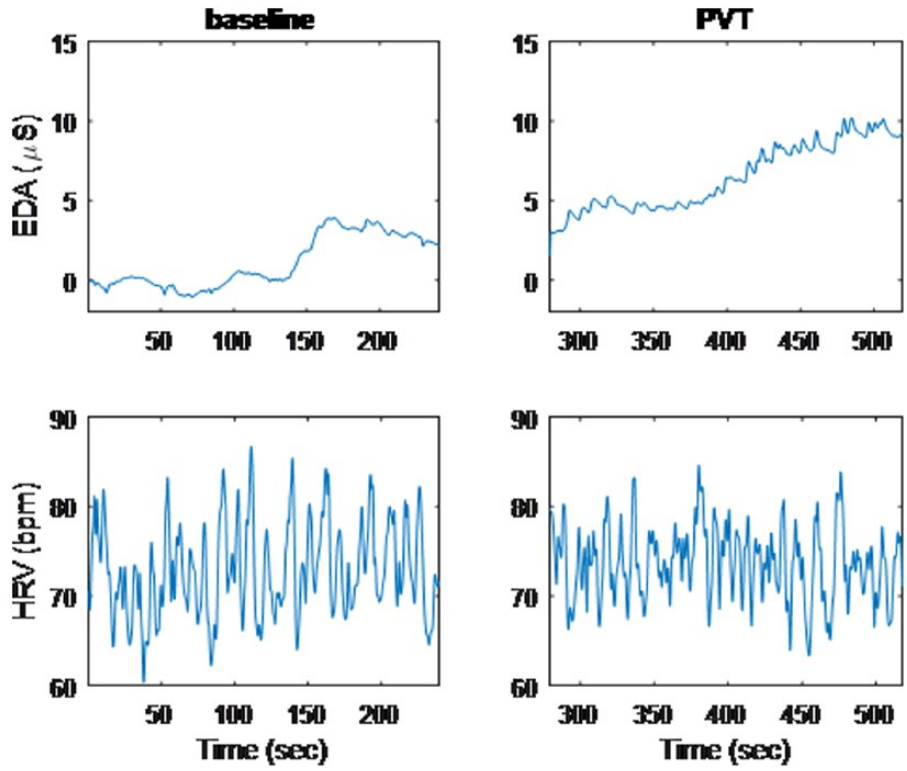

Figure 1. EDA (top) and HRV (bottom) data during baseline (left) and PVT task (right) stages, for a given participant and trial.

Statistics

The physiological measures of the ANS obtained in this study include SCL, NSSCRs, EDASymp, TVSymp, HRVLF, HRVLFn, HRVHF, and HRVHFn. To assess participants' performance during every trial, four indices were computed based on RT measures and false starts: average reaction time (avRT), total amount of minor lapses (RT > 500 ms), major lapses (RT > 1 s), and false starts during the PVT. Among the many possible measures that can be obtained from PVT trials, the number of minor lapses is often used as the primary dependent variable in testing the performance deterioration under prolonged wakefulness (Lim & Dinges, 2008). All four indices are inversely correlated to participants' performance (e.g., higher avRT represents lower performance).

Repeated measurements analysis was deployed to evaluate the significance of differences in the indices of HRV, EDA, and PVT between trials, due to sleep deprivation. Normality of the EDA and HRV indices throughout the 12 trials was tested using the one-sample Kolmogorov-Smirnov test (Massey, 1951; Miller, 1956; Wang, Tsang, & Marsaglia, 2003). If nonnormality was found, nonparametric statistical techniques were used.

For repeated measurements analysis in normally distributed data, the one-way analysis of variance (ANOVA) was performed to test for significant differences between trials. When data were nonnormally distributed, we used the Friedman test (Friedman, 1937), a nonparametric statistical test similar to the parametric repeated-measures ANOVA. The Bonferroni method was used for correction of multiple comparisons.

Correlation coefficients between mean values of PVT measures (avRT, minor lapses, major lapses, and false starts) and measures of ANS (indices of EDA and HRV) of the participants (over the 12 runs, 24-hour test) were computed. Pearson's correlation coefficient (r) was used for

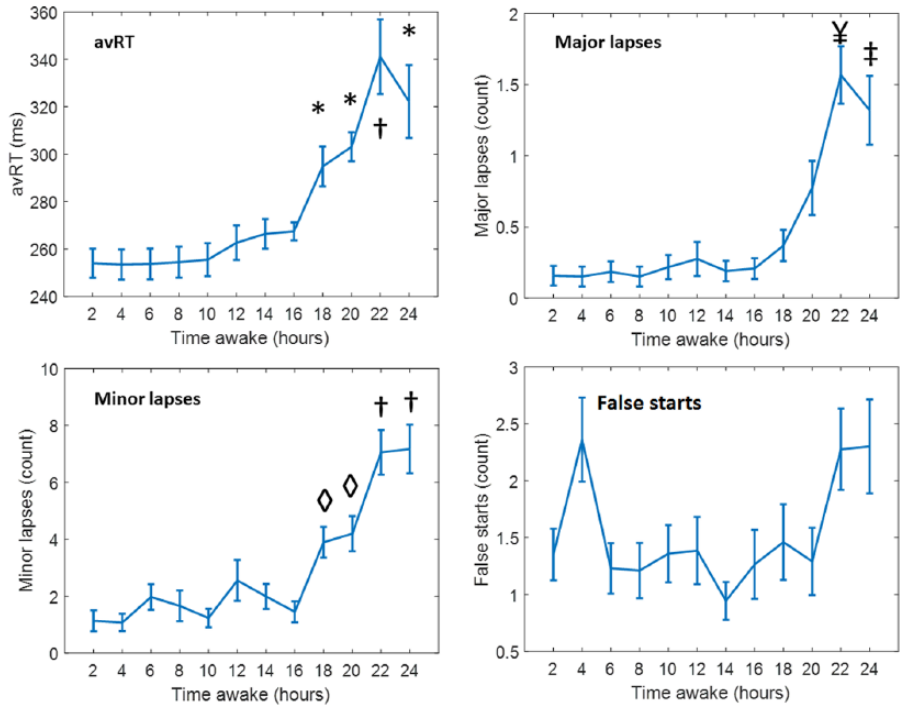

Figure 2. Indices of performance in PVT. Mean value ± SEM for avRT, major lapses, minor lapses, and false start values obtained during the 24-hour period of sleep deprivation. Symbols indicate significant difference: * to Trials 1 to 5; † to Trials 1 to 8; ¥ to Trials 1 to 9; ‡ to Trials 1 to 7; ◊ to Trials 1, 2, 4, 5, and 8.

avRT, as it was normally distributed. As major lapses, minor lapses, and false starts indices were found nonnormally distributed, Spearman's (r_s) correlation coefficient was used. The *t* test was used to assess the statistical significance of correlation coefficient (the null hypothesis was that the product moment correlation coefficient was zero) (Spiegel, 1961).

For evaluating the suitability of the indices of ANS to detect the effects of prolonged wakefulness, the receiver operating characteristic (ROC) curve was computed for each index of ANS (Metz, 1978). For this, the values of the indices of performance above the mean plus 1 *SD* (for each individual participant) were considered as instances of performance deterioration (Class 1). All other values were considered normal (Class 0). To assess the performance of the detectors, the area under the curve (AUC) (an estimate of the probability that a specific index will assign to a positive instance a higher value than to a negative) was computed for each ROC curve (Hanley & McNeil, 1982).

RESULTS

Indices of performance and noninvasive measures of ANS obtained during the 24-hour sleep deprivation period are shown in Figures 2, 3, and 4. The figures display the mean ± standard error of the mean (SEM) for PVT, HRV, and EDA indices, respectively. SCL, TVSymp, HRVLF, HRVLFn, HRVHF, HRVHFn, minor lapses, and false starts were found normally distributed throughout the 12 trials. NSSCRs, EDASymp, and major lapses did not meet the normality criteria. Multicomparison tests exhibited statistically significant effects of sleep deprivation in avRT, major lapses, minor lapses, HRVHFn, and TVSymp. Significant differences between trials are marked in the figures.

AvRT exhibits high variability with time during the first 16 hours of the experiment, followed by an increase starting after 18 hours of sleep deprivation. The maximum deterioration of avRT (minimum performance) was observed during the trial at 22 hours. Major lapses were stable during the first 20 hours of the experiment

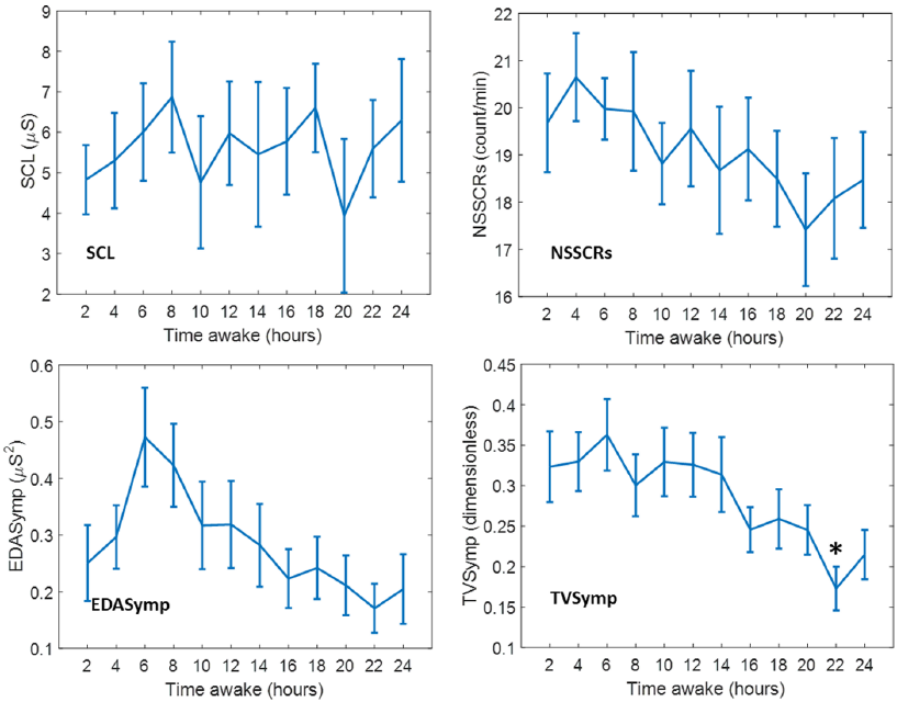

Figure 3. Indices of EDA. Mean value ± SEM for SCL, NSSCRs, EDASymp, and TVSymp obtained during the 24-hour period of sleep deprivation. Symbols indicate significant difference: * to Trial 3.

and then exhibited an increase after 22 hours. Minor lapses were stable during the first 16 hours, except for an increase at 12 hours, and also increased by the end of the experiment (22 hours). False starts were particularly high during the second trial, then stabilized to lower values with a minimum at 14 hours, and then increased for the remainder of the experiment.

As for the indices of EDA, changes in SCL were not as sensitive an indicator of performance deterioration (PVT measures). SCL exhibited a stable value throughout the experiment, with a decrease at Hour 20, followed by a recovery to initial values. However, frequency of NSSCRs index was more sensitive than SCL as it was stable during the first 18 hours of the experiment, with an increase at 12 hours, and then a decrease in value after 20 hours. Similarly, EDASymp exhibited an increase during the first three trials, then exhibited decreased values until 18 hours, and showed another decrease after 20 hours. TVSymp was the most sensitive as it was stable during the first 12 hours, then decreased for Trials 7 (14 hours) through 10 (20 hours), and presented a significant decrease at Trial 11 (22 hours), compared to Trial 3 (6 hours).

HRVLF showed a trend of increase at the 4th hour, remained stable until Trial 4 (8th hour), then showed a trend of decrease at the 10th hour, and had a noticeable increase at 22 hours. HRVLFn showed decreases and increases during the 24-hour period. It exhibited minima at 12 hours, 18 hours, and 24 hours and maxima at 4, 14, and 20 hours. HRVHF decreased at 4 hours, then was stable until 8 hours, then decreased until reaching a minimum at 14 hours, and recovered to higher values toward the end of the experiment. HRVHFn was similar, but opposite, to HRVLFn. It exhibited minima at 4, 12, and 22 hours and maxima at 10 and 20 hours. Significant differences in HRVHFn were found in Trials 11 (with respect to Trials 1 and 5) and 12 (with respect to Trial 1).

Table 1 includes the results of correlation and detection analysis. In total, 32 correlations were computed between indices of ANS (HRV and EDA) and performance, and 32 detector

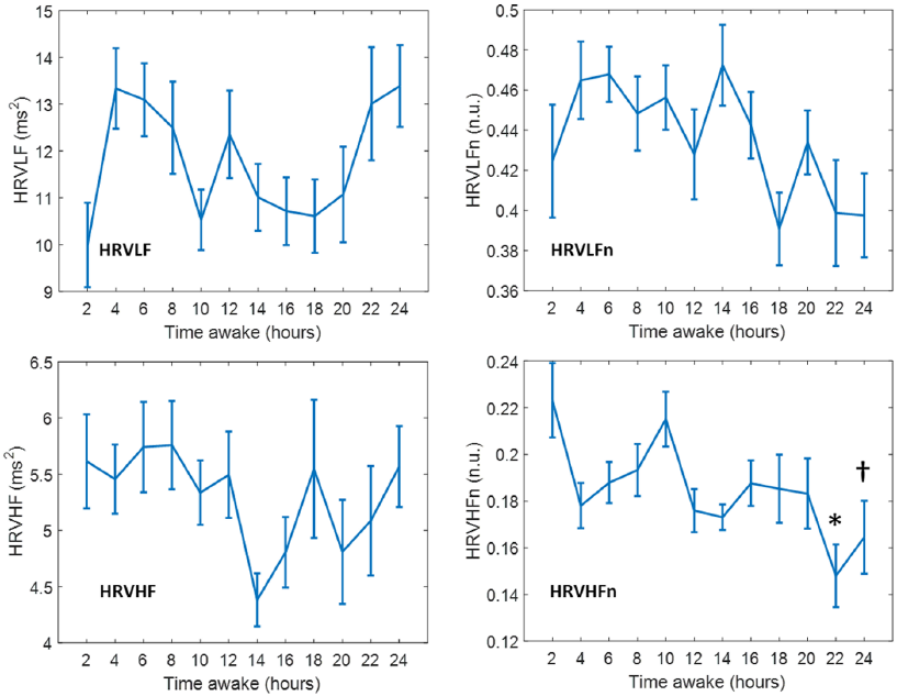

Figure 4. Indices of HRV. Mean value ± SEM for HRVLF, HRVLFn, HRVHF, and HRVHFn obtained during the 24-hour period of sleep deprivation. Symbols indicate significant difference: * to Trials 1 and 5; † to Trial 1.

performances were evaluated using the ROC AUC. TVSymp exhibited the highest statistically significant correlation to avRT, major lapses, and minor lapses (–0.92, –0.85, and –0.83, respectively). NSSCRs and HRVLFn also exhibited statistically significant correlation to those three measures of PVT, although lower than that of TVSymp. HRVHFn was moderately correlated to minor lapses. As for detection analysis as quantified by the ROC, TVSymp exhibited the highest AUC value for avRT (0.74), major lapses (0.72), and false starts (0.59), whereas AUC for HRVLFn was slightly higher for minor lapses (0.69), compared to TVSymp (0.68). Figure 5 includes the scatterplots of the raw data for the significant correlations found between indices of ANS and indices of performance.

DISCUSSION

We have observed that TVSymp, an index accounting for higher frequencies of EDA, was strongly correlated to indices of performance in PVT. Other measures like NSSCRs, HRVLFn, HRVLF, and HRVHF exhibited lower correlation, whereas other indices did not show significant correlation. Furthermore, TVSymp was the most sensitive detector of the deterioration of performance. This suggests that the effects of sleep deprivation on autonomic response were more noticeable at the skin level than at the cardiac level. Assessment techniques using information from both HRV and EDA provide central and peripheral noninvasive autonomic assessment, respectively. Based on our results, EDA can potentially assess and predict the effect of prolonged wakefulness in the autonomic response and task performance of individuals, which can then be used to prevent unfortunate (usually fatal) consequences.

HRV has been widely used to understand the effects of sleep deprivation. However, results have been inconclusive. In a past study, a group of volunteers were kept awake for 40 hours performing a constant routine; the authors found that HRV was generally reduced after prolonged wakefulness (Viola et al., 2008). These results

TABLE 1: Correlation and Detection Analysis

		avRT		Major Lapses		Minor Lapses		False Starts	
		r	AUC	r_s	AUC	r_s	AUC	r_s	AUC
EDA	SCL	0.21	0.48	0.25	0.50	0.24	0.44	0.24	0.50
	NSSCR	–0.80*	0.60	–0.71*	0.64	–0.65*	0.65	–0.45	0.45
	EDASymp	–0.24	0.66	–0.19	0.64	–0.19	0.63	0.03	0.56
	TVSymp	–0.92**	0.74	–0.85**	0.72	–0.83**	0.68	–0.57	0.59
HRV	HRVLF	0.33	0.45	0.33	0.49	0.35	0.44	0.59	0.44
	HRVLFn	–0.77*	0.68	–0.66*	0.69	–0.64*	0.69	–0.53	0.56
	HRVHF	0.26	0.51	0.28	0.53	0.32	0.44	0.2	0.37
	HRVHFn	–0.57	0.70	–0.56	0.69	–0.58*	0.56	–0.48	0.44

Note. AUC = area under the curve of the ROC curve; EDASymp = sympathetic component of the EDA; HRVLF = low-frequency components of heart rate variability (HRV); HRVLFn = normalized low-frequency components of HRV; NSSCRs = nonspecific skin conductance responses; r = Pearson's correlation coefficient; r_s = Spearman's correlation coefficient; SCL = skin conductance level; TVSymp = time-varying index of sympathetic tone.
*$p < .05$. **$p < .001$.

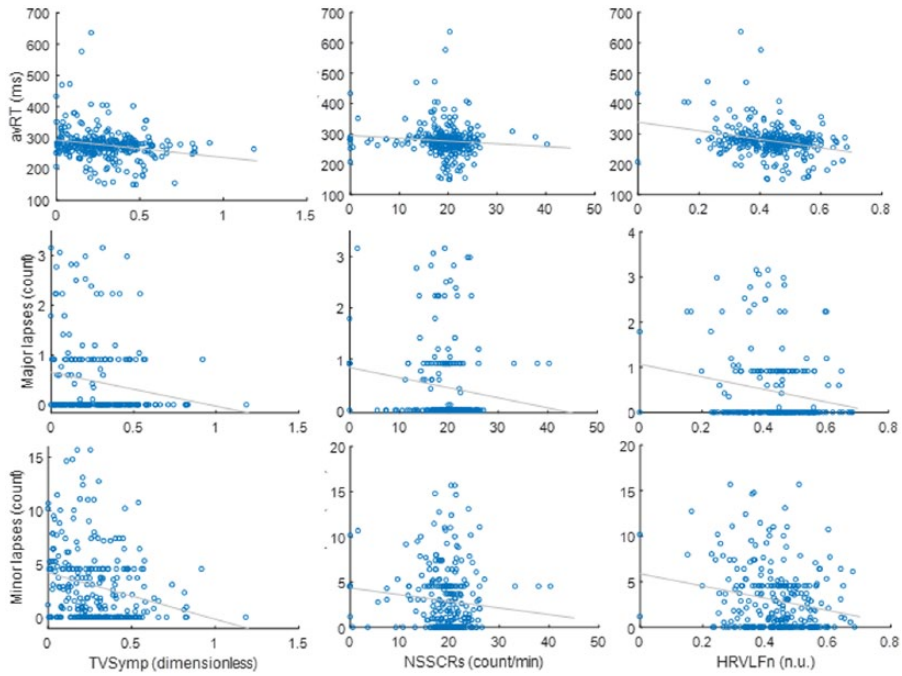

Figure 5. Scatterplots of the raw data for correlation analysis. Top row: avRT; middle row: major lapses; bottom row: minor lapses; left column: TVSymp; center column: NSSCRs; right column: HRVLFn.

revealed a smaller decline in HRV due to prolonged wakefulness, compared to sleeping conditions. Another group of participants underwent 36 hours of wakefulness, revealing an increase in sympathetic autonomic modulation and a decrease in parasympathetic autonomic modulation during daytime (Zhong et al., 2005). In this study, they found diminished spectral indices of

HRV for healthy participants performing a repetitive cognitive test. Another study did not find a significant increase in sympathetic modulation during daytime (diminished overall HRV) after one night of wakefulness (Pagani et al., 2009). Other researchers found a moderate correlation of spectral indices of HRV with participants' performance in PVT during sleep deprivation (Chua et al., 2012). In our previous study (Posada-Quintero et al., 2017), few significant differences were found in HRV parameters throughout the experiment. Only HRVLF exhibited a significant increase after 20 hours. Although results look opposite to the present study, the test implemented was different and its effects on ANS are also distinct.

Literature on the effect of sleep deprivation using EDA as a measure is not ample. The literature provides inconsistent results on changes in the slow and phasic shifts of EDA during sleep deprivation but highlights the methodological limitations of these studies (single case studies, measurements taken only once or twice during the test, or lack of statistical analysis) (Horne, 1978). Another study found an increase in latency and reduction in amplitude of event-elicited SCRs after 36 hours of sleep deprivation, but PVT was not measured (McCarthy & Waters, 1997). Using a simple RT test, a recent study reported a correlation in the reduction of SCL and the impairment of the RT (Miró et al., 2002). Another study examined how the sympathetic nervous system (assessed using the SCL) contributes to altered reactiveness in sleep-deprived persons (Liu et al., 2015). The latter two studies only analyzed the slow shifts represented in the SCL. Additionally, in our recent study involving healthy participants who underwent cognitive stress tests post-24-hour sleep deprivation, we found statistically significant changes in the indices that represent higher frequencies of EDA (NSSCRs, EDASymp, and TVSymp), not present in the LF shifts in level (SCL) (Posada-Quintero et al., 2017). For these studies, the above mentioned SCL and SCR indices of EDA were not directly compared to PVT, as the latter data were not simultaneously acquired.

In the present study, we found a strong correlation between three of the obtained indices of performance of PVT and TVSymp. TVSymp incorporates both frequency- and time-domain information of EDA in one index. In particular, TVSymp's high correlation to avRT, major lapses, and minor lapses indicates that it can be used to detect the deterioration in performance produced by sleep deprivation (higher than 0.83). Among EDA indices, we found the weakest correlation of SCL and EDASymp to the indices of performance. Indices of HRV exhibited moderate absolute correlation, with a maximum value of 0.68. These differences of correlation of the indices of EDA and HRV to performance measures provide evidence that the effects of sleep deprivation on the autonomic response are stronger at the peripheral level than at the central level. We can also speculate that the reduction of fast sympathetic innervation at the skin level produced by prolonged wakefulness (at least during a 24-hour period), observable in the higher frequency components of the EDA signal, causes a decrease in humans' capacity to react in a timely manner.

HF components of EDA are known to be evoked by central (hypothalamus, medulla) or peripheral (pre- and postganglionic peripheral nerve) mechanisms (Koss & Davison, 1976) and have been linked to attention and stimulus novelty (Hochberg, Kling, & Riggs, 1971). TVSymp more sensitively captures this effect, as it comprises both the time and frequency dynamics of EDA in a single measure. TVSymp has been shown to be a sensitive measure of arousal caused by different stressors, including physical and cognitive (Posada-Quintero, Florian, Orjuela-Cañón, & Chon, 2016). As HRV only reflects the dynamics of ANS, it is not as sensitive for detecting such decreases in RT, in comparison with TVSymp, for example.

It is expected that PVT, EDA, and HRV indices measured during a 24-hour period of wakefulness were sensitive to both circadian rhythms and sleep deprivation. Nevertheless, it is known that sleep deprivation causes an overall increase of RTs and increased errors of omission and commission (Lim & Dinges, 2008). In fact, this is the effect we observe on the measures of performance of PVT collected in this study (Figure 2), as there was a significant trend of increasing RT and decreasing accuracy toward the end of the 24-hour period. In the top panels of Figure 2,

the first data points were collected after 2 hours of testing and the last 3 data points were taken after the participant was awake for at least 18 hours. By then, usually 4 to 8 AM, effects of the circadian rhythm would cause a decrease in the RT. Instead, we observed in Figure 3 a continued trend of increase in the RT, lapses, and false starts. Hence, such a trend with consistent increase in sleep deprivation indicates that participants are more affected by sleep deprivation than by the circadian rhythm. Similar results can be seen in some indices of EDA (NSSCRs, EDASymp, and TVSymp; Figure 3), with the same interpretation. It should be noted that we do observe a recovery (increase) in those indices in the panels of Figure 3 at 24 hours, which is likely due to the circadian effect. In the PVT measures, toward the end of the experiment (Trial 12), there is recovery or return to low values (better performance). This may suggest that in addition to possible circadian effects, the participants may have tried to stay focused and vigilant, causing a "final spurt," which was noticeable in both PVT and some ANS measures (Figures 2, 3, and 4).

In this study, we computed NSSCRs automatically utilizing the convex optimization approach (Greco et al., 2016). There are other automatic ways to count spontaneous SCRs, extract amplitude or other measures of a single causal SCR, and deal with motion artifacts and superposition on the SCRs (Bach & Friston, 2013; Benedek & Kaernbach, 2010; Chaspari, Tsiartas, Stein, Cermak, & Narayanan, 2015). However, the spectral and time-varying indices utilize widely implemented and relatively simple digital-processing techniques and do not rely on either manual or automatic SCR detection, which is usually more complex and time consuming.

CONCLUSION

We studied the effects of prolonged wakefulness on human performance and autonomic response. Participants performed the standardized PVT task every 2 hours during a 24-hour period, and indices of EDA and HRV were collected during every trial. We found high correlation between the most relevant indices for assessing performance in PVT (avRT, major lapses, and minor lapses), and the physiological index of EDA that represents higher frequencies of the signal, TVSymp. We conclude that this index of EDA can be used for creating or improving techniques to assess and predict impaired cognitive performance and prevent consequences caused by the effects of prolonged wakefulness.

ACKNOWLEDGMENTS

This work was supported by the Office of Naval Research work unit N00014-15-1-2236. M. Qin is an employee of the U.S. Government. This work was prepared as part of his official duties. Title 17 U.S.C. §105 provides that "Copyright protection under this title is not available for any work of the United States Government." Title 17 U.S.C. §101 defines a U.S. Government work as a work prepared by a military service member or employee of the U.S. Government as part of that person's official duties. The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the U.S. Government.

KEY POINTS

- Measurements of performance of PVT in sleep-deprived participants collected in this study were consistent with those previously reported in the literature.
- The SCL (slow shifts of EDA), the power spectral index (EDASymp), and the HF components of HRV (HRVHF and HRFHFn) did not show significant correlations to the measurements of performance of PVT.
- The NSSCRs, the time-varying index of EDA (TVSymp), and normalized LF components of HRV (HRVLFn) were significantly correlated to measurements of performance ($p < .05$).
- TVSymp exhibited the highest correlation to avRT (–0.92), major lapses (–0.85), and minor lapses (–0.83) ($p < .001$).
- Indices that account for HF dynamics in the EDA, specially the TVSymp, constitute a valuable tool for understanding the changes in the ANS and detect the effects of prolonged wakefulness on human performance.

ORCID ID

Hugo F. Posada-Quintero https://orcid.org/0000-0003-4514-4772

REFERENCES

Appenzeller, O. (1987). The autonomic nervous system and fatigue. *Functional Neurology*, *2*(4), 473–485.

Bach, D. R., & Friston, K. J. (2013). Model-based analysis of skin conductance responses: Towards causal models in psychophysiology. *Psychophysiology*, *50*(1), 15–22.

Baharav, A., Kotagal, S., Gibbons, V., Rubin, B. K., Pratt, G., Karin, J., & Akselrod, S. (1995). Fluctuations in autonomic nervous activity during sleep displayed by power spectrum analysis of heart rate variability. *Neurology*, *45*(6), 1183–1187.

Benedek, M., & Kaernbach, C. (2010). A continuous measure of phasic electrodermal activity. *Journal of Neuroscience Methods*, *190*(1–5), 80–91. https://doi.org/10.1016/j.jneumeth.2010.04.028

Boucsein, W. (2012). *Electrodermal activity*. Boston, MA: Springer. Retrieved from http://link.springer.com/10.1007/978-1-4614-1126-0

Boucsein, W., Fowles, D. C., Grimnes, S., Ben-Shakhar, G., Roth, W. T., Dawson, M. E., . . . Society for Psychophysiological Research Ad Hoc Committee on Electrodermal Measures. (2012). Publication recommendations for electrodermal measurements. *Psychophysiology*, *49*(8), 1017–1034. https://doi.org/10.1111/j.1469-8986.2012.01384.x

Chaspari, T., Tsiartas, A., Stein, L. I., Cermak, S. A., & Narayanan, S. S. (2015). Sparse representation of electrodermal activity with knowledge-driven dictionaries. *IEEE Transactions on Biomedical Engineering*, *62*(3), 960–971.

Chon, K. H., Dash, S., & Ju, K. (2009). Estimation of respiratory rate from photoplethysmogram data using time-frequency spectral estimation. *IEEE Transactions on Bio-Medical Engineering*, *56*(8), 2054–2063. https://doi.org/10.1109/TBME.2009.2019766

Chua, E. C.- P., Tan, W.- Q., Yeo, S.- C., Lau, P., Lee, I., Mien, I. H., . . . Gooley, J. J. (2012). Heart rate variability can be used to estimate sleepiness-related decrements in psychomotor vigilance during total sleep deprivation. *SLEEP*. https://doi.org/10.5665/sleep.1688

Colbert, A. P., Spaulding, K., Larsen, A., Ahn, A. C., & Cutro, J. A. (2011). Electrodermal activity at acupoints: Literature review and recommendations for reporting clinical trials. *Journal of Acupuncture and Meridian Studies*, *4*(1), 5–13. https://doi.org/10.1016/S2005-2901(11)60002-2

Cooke, W. H., Salinas, J., Convertino, V. A., Ludwig, D. A., Hinds, D., Duke, J. H., . . . Holcomb, J. B. (2006). Heart rate variability and its association with mortality in prehospital trauma patients. *The Journal of Trauma*, *60*(2), 363–370; discussion 370. https://doi.org/10.1097/01.ta.0000196623.48952.0e

Costa, G. (1996). The impact of shift and night work on health. *Applied Ergonomics*, *27*(1), 9–16.

Dawson, M. E., Schell, A. M., & Filion, D. L. (2007). The electrodermal system. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of psychophysiology* (3rd ed., pp. 159–181). Cambridge, UK: Cambridge University Press.

Dinges, D. F. (1995). An overview of sleepiness and accidents. *Journal of Sleep Research*, *4*(S2), 4–14.

Dorrian, J., Rogers, N. L., & Dinges, D. F. (2005). *Psychomotor vigilance performance: Neurocognitive assay sensitive to sleep loss*. New York, NY: Marcel Dekker. Retrieved from http://faculty.vet.upenn.edu/uep/assets/user-content/documents/DorrianetalPVTchapterinKushida2005.pdf

Fogt, D. L., Cooke, W. H., Kalns, J. E., & Michael, D. J. (2011). Linear mixed-effects modeling of the relationship between heart rate variability and fatigue arising from sleep deprivation. *Aviation, Space, and Environmental Medicine*, *82*(12), 1104–1109. https://doi.org/10.3357/ASEM.3014.2011

Fogt, D. L., Kalns, J. E., & Michael, D. J. (2010). A comparison of cognitive performance decreases during acute, progressive fatigue arising from different concurrent stressors. *Military Medicine*, *175*(12), 939–944.

Freeman, R., & Chapleau, M. W. (2013). Testing the autonomic nervous system. *Handbook of Clinical Neurology*, 115, 115–136.

Friedman, M. (1937). The use of ranks to avoid the assumption of normality implicit in the analysis of variance. *Journal of the American Statistical Association*, *32*(200), 675–701. https://doi.org/10.1080/01621459.1937.10503522

Fullagar, H. H. K., Skorski, S., Duffield, R., Hammes, D., Coutts, A. J., & Meyer, T. (2015). Sleep and athletic performance: The effects of sleep loss on exercise performance, and physiological and cognitive responses to exercise. *Sports Medicine (Auckland, N.Z.)*, *45*(2), 161–186. https://doi.org/10.1007/s40279-014-0260-0

Furman, G. D., Baharav, A., Cahan, C., & Akselrod, S. (2008). Early detection of falling asleep at the wheel: A Heart Rate Variability approach. In *2008 Computers in Cardiology* (pp. 1109–1112). Piscataway, NJ: Institute of Electrical and Electronics Engineers. https://doi.org/10.1109/CIC.2008.4749240

Glos, M., Fietze, I., Blau, A., Baumann, G., & Penzel, T. (2014). Cardiac autonomic modulation and sleepiness: Physiological consequences of sleep deprivation due to 40 h of prolonged wakefulness. *Physiology & Behavior*, *125*, 45–53. https://doi.org/10.1016/j.physbeh.2013.11.011

Greco, A., Valenza, G., Lanata, A., Scilingo, E. P., & Citi, L. (2016). cvxEDA: A convex optimization approach to electrodermal activity processing. *IEEE Transactions on Biomedical Engineering*, *63*(4), 797–804.

Hanley, J. A., & McNeil, B. J. (1982). The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology*, *143*(1), 29–36. https://doi.org/10.1148/radiology.143.1.7063747

Hochberg, J., Kling, J. W., & Riggs, L. A. (1971). *Woodworth & Schlosberg's experimental psychology*. New York, NY: Holt, Rinehart, & Winston.

Horne, J. A. (1978). A review of the biological effects of total sleep deprivation in man. *Biological Psychology*, *7*(1–2), 55–102.

Izawa, S., Sugaya, N., Yamamoto, R., Ogawa, N., & Nomura, S. (2010). The cortisol awakening response and autonomic nervous system activity during nocturnal and early morning periods. *Neuro Endocrinology Letters*, *31*(5), 685–689.

Khitrov, M. Y., Laxminarayan, S., Thorsley, D., Ramakrishnan, S., Rajaraman, S., Wesensten, N. J., & Reifman, J. (2014). PC-PVT: A platform for psychomotor vigilance task testing, analysis, and prediction. *Behavior Research Methods*, *46*(1), 140–147. https://doi.org/10.3758/s13428-013-0339-9

Koss, M. C., & Davison, M. A. (1976). Characteristics of the electrodermal response. A model for analysis of central sympathetic reactivity. *Naunyn-Schmiedeberg's Archives of Pharmacology*, *295*(2), 153–158.

Leger, D. (1994). The cost of sleep-related accidents: A report for the National Commission on Sleep Disorders Research. *Sleep*, *17*(1), 84–93.

Lim, J., & Dinges, D. F. (2008). Sleep deprivation and vigilant attention. *Annals of the New York Academy of Sciences*, *1129*, 305–322. https://doi.org/10.1196/annals.1417.002

Liu, J. C. J., Verhulst, S., Massar, S. A. A., & Chee, M. W. L. (2015). Sleep deprived and sweating it out: The effects of total sleep deprivation on skin conductance reactivity to psychosocial stress. *Sleep*, *38*(1), 155–159. https://doi.org/10.5665/sleep.4346

Lyznicki, J. M., Doege, T. C., Davis, R. M., & Williams, M. A. (1998). Sleepiness, driving, and motor vehicle crashes. Council

on Scientific Affairs, American Medical Association. *JAMA*, *279*(23), 1908–1913.

Massey, F. J., Jr. (1951). The Kolmogorov-Smirnov test for goodness of fit. *Journal of the American Statistical Association*, *46*(253), 68–78.

McCarthy, M. E., & Waters, W. F. (1997). Decreased attentional responsivity during sleep deprivation: Orienting response latency, amplitude, and habituation. *Sleep*, *20*(2), 115–123.

Metz, C. E. (1978). Basic principles of ROC analysis. *Seminars in Nuclear Medicine*, *8*(4), 283–298.

Michail, E., Kokonozi, A., Chouvarda, I., & Maglaveras, N. (2008). EEG and HRV markers of sleepiness and loss of control during car driving. *Conference Proceedings: ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference*, *2008*, 2566–2569. https://doi.org/10.1109/IEMBS.2008.4649724

Miller, L. H. (1956). Table of percentage points of Kolmogorov statistics. *Journal of the American Statistical Association*, *51*(273), 111–121.

Miró, E., Cano-Lozano, M. C., & Buela-Casal, G. (2002). Electrodermal activity during total sleep deprivation and its relationship with other activation and performance measures. *Journal of Sleep Research*, *11*(2), 105–112.

Nakano, T., Araki, K., Michimori, A., Inbe, H., Hagiwara, H., & Koyama, E. (2000). Temporal order of sleepiness, performance and physiological indices during 19-h sleep deprivation. *Psychiatry and Clinical Neurosciences*, *54*(3), 280–282. https://doi.org/10.1046/j.1440-1819.2000.00678.x

Nygaards, M.- E., & Sörnmo, L. (1983). Delineation of the QRS complex using the envelope of the ECG. *Medical and Biological Engineering and Computing*, *21*(5), 538–547.

Pagani, M., Pizzinelli, P., Traon, A. P.- L., Ferreri, C., Beltrami, S., Bareille, M.- P., . . . Philip, P. (2009). Hemodynamic, autonomic and baroreflex changes after one night sleep deprivation in healthy volunteers. *Autonomic Neuroscience: Basic & Clinical*, *145*(1–2), 76–80. https://doi.org/10.1016/j.autneu.2008.10.009

Posada-Quintero, H. F., Bolkhovsky, J. B., Reljin, N., & Chon, K. H. (2017). Sleep deprivation in young and healthy subjects is more sensitively identified by higher frequencies of electrodermal activity than by skin conductance level evaluated in the time domain. *Frontiers in Physiology*, *8*, 1–9. https://doi.org/10.3389/fphys.2017.00409

Posada-Quintero, H. F., Florian, J. P., Orjuela-Cañón, A. D., Aljama-Corrales, T., Charleston-Villalobos, S., & Chon, K. H. (2016). Power spectral density analysis of electrodermal activity for sympathetic function assessment. *Annals of Biomedical Engineering*, *44*(10), 3124–3135. https://doi.org/10.1007/s10439-016-1606-6

Posada-Quintero, H. F., Florian, J. P., Orjuela-Cañón, Á. D., & Chon, K. H. (2016). Highly sensitive index of sympathetic activity based on time-frequency spectral analysis of electrodermal activity. *American Journal of Physiology–Regulatory, Integrative and Comparative Physiology*, *311*(3), R582–R591. https://doi.org/10.1152/ajpregu.00180.2016

Spiegel, M. R. (1961). *Statistics: Schaum's outline series in mathematics*. New York, NY: McGraw-Hill.

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. (1996). Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, *17*(3), 354–381.

Tobaldini, E., Cogliati, C., Fiorelli, E. M., Nunziata, V., Wu, M. A., Prado, M., . . . Montano, N. (2013). One night on-call: Sleep deprivation affects cardiac autonomic control and inflammation in physicians. *European Journal of Internal Medicine*, *24*(7), 664–670. https://doi.org/10.1016/j.ejim.2013.03.011

Vicente, J., Laguna, P., Bartra, A., & Bailón, R. (2016). Drowsiness detection using heart rate variability. *Medical & Biological Engineering & Computing*, *54*(6), 927–937. https://doi.org/10.1007/s11517-015-1448-7

Vidaurre, C., Sander, T. H., & Schlögl, A. (2011). BioSig: The free and open source software library for biomedical signal processing. *Computational Intelligence and Neuroscience*, *2011*, 935364. https://doi.org/10.1155/2011/935364

Viola, A. U., James, L. M., Archer, S. N., & Dijk, D.- J. (2008). PER3 polymorphism and cardiac autonomic control: Effects of sleep debt and circadian phase. *American Journal of Physiology. Heart and Circulatory Physiology*, *295*(5), H2156–H2163. https://doi.org/10.1152/ajpheart.00662.2008

Wang, J., Tsang, W. W., & Marsaglia, G. (2003). Evaluating Kolmogorov's distribution. *Journal of Statistical Software*, *8*(18).

Winchell, R. J., & Hoyt, D. B. (1997). Analysis of heart-rate variability: A noninvasive predictor of death and poor outcome in patients with severe head injury. *The Journal of Trauma*, *43*(6), 927–933.

Zar, J. H. (1999). *Biostatistical analysis: Pearson education India*. New Delhi, India: Prentice Hall.

Zhong, X., Hilton, H. J., Gates, G. J., Jelic, S., Stern, Y., Bartels, M. N., . . . Basner, R. C. (2005). Increased sympathetic and decreased parasympathetic cardiovascular modulation in normal humans with acute sleep deprivation. *Journal of Applied Physiology*, *98*(6), 2024–2032. https://doi.org/10.1152/jap plphysiol.00620.2004

Hugo F. Posada-Quintero is a postdoctoral research associate at the Department of Biomedical Engineering at the University of Connecticut. He received his PhD in Biomedical Engineering from the University of Connecticut in 2016.

Jeffrey B. Bolkhovsky was a PhD student at the University of Connecticut at the time this study was conducted. After receiving his PhD in Biomedical Engineering from the University of Connecticut, he joined the Naval Submarine Medical Research Laboratory as a Research Scientist.

Michael Qin was a principal investigator at the Naval Submarine Medical Research Laboratory at the time of his participation in this study. Currently, he is a program officer at the Office of Naval Research. He received his PhD in Psychophysics from the Harvard-MIT Division of Health Sciences and Technology in 2004.

Ki H. Chon is a chair professor and Head of Biomedical Engineering at University of Connecticut. He received his PhD in Biomedical Engineering from the University of Southern California in 1993.

Date received: January 16, 2018
Date accepted: May 14, 2018