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SLEEP COGNITION AND BEHAVIOR

A Unified Model of Performance: Validation of its Predictions across Different Sleep/Wake Schedules

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Study Objectives: Historically, mathematical models of human neurobehavioral performance developed on data from one sleep study were limited to predicting performance in similar studies, restricting their practical utility. We recently developed a unified model of performance (UMP) to predict the effects of the continuum of sleep loss—from chronic sleep restriction (CSR) to total sleep deprivation (TSD) challenges—and validated it using data from two studies of one laboratory. Here, we significantly extended this effort by validating the UMP predictions across a wide range of sleep/wake schedules from different studies and laboratories.

Methods: We developed the UMP on psychomotor vigilance task (PVT) lapse data from one study encompassing four different CSR conditions (7 d of 3, 5, 7, and 9 h of sleep/night), and predicted performance in five other studies (from four laboratories), including different combinations of TSD (40 to 88 h), CSR (2 to 6 h of sleep/night), control (8 to 10 h of sleep/night), and nap (nocturnal and diurnal) schedules.

Results: The UMP accurately predicted PVT performance trends across 14 different sleep/wake conditions, yielding average prediction errors between 7% and 36%, with the predictions lying within 2 standard errors of the measured data 87% of the time. In addition, the UMP accurately predicted performance impairment (average error of 15%) for schedules (TSD and naps) not used in model development.

Conclusions: The unified model of performance can be used as a tool to help design sleep/wake schedules to optimize the extent and duration of neurobehavioral performance and to accelerate recovery after sleep loss.

Keywords: biomathematical model, chronic sleep restriction, naps, PVT, total sleep deprivation, two-process model

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Significance

We showed that, given the sleep/wake schedule of a group of individuals, one mathematical model can accurately predict neurobehavioral performance across a whole host of sleep-loss conditions, including conditions considerably different from those used in model development. In particular, the model accurately predicted the effects of sleep loss (total and partial) and countermeasure strategies, such as extended sleep and short daytime sleep episodes, with errors in model predictions no greater than those observed in the experimental performance data. Such a validated model can be used to generate hypotheses that can be experimentally tested, and to design optimal sleep/wake schedules for maintaining performance at desired levels at specified times of the day or for accelerating recovery following sleep loss.

INTRODUCTION

Borbely's[1] seminal two-process model of sleep regulation provides an elegant mathematical representation of the temporal dynamics of homeostatic and circadian sleep processes. These two processes also account for the bulk of the variation in neurobehavioral performance both within and across days and, therefore, serve as the theoretical framework for most neurobehavioral performance prediction models.[2] However, although such models performed well when applied to humans exposed to total sleep deprivation (TSD) conditions, they were less accurate for predicting the effects of chronic sleep restriction (CSR) because they do not account for prior sleep/wake history[3] and inaccurately specify the relationship between the lower and upper asymptotes of the homeostatic sleep process.[4]

Recently, to address these issues, we developed a unified model of performance (UMP), which captures the neurobehavioral performance effects of both TSD and CSR in a single (i.e., unified) mathematical model.[5] The UMP was able to reproduce physiological findings, which showed that neurobehavioral performance recovery following sleep loss is inversely proportional to sleep debt[6] and that extending sleep prior to CSR slows performance degradation and results in faster subsequent recovery.[7] Although the UMP accurately predicted neurobehavioral performance for two studies (involving 64 h of TSD and CSR of 7 nights with 3 h of sleep/night)[7,8] from one laboratory, before it can be broadly applied, its performance must be validated across a larger number of studies, encompassing a wider range of sleep/wake schedules, including different durations of TSD and CSR and their combinations. In addition, it must show the ability to predict performance under sleep/wake schedules not used in developing the model. Furthermore, because the UMP has only been validated on studies from one research group, whether its predictions are generalizable across laboratories remains unknown. Therefore, in the current work, our first objective was to:

1. Determine the extent to which the UMP developed from the results of one study (composed of four different sleep/wake conditions) accurately predicts results obtained from five different studies in four different laboratories, comprising a total of 14 different sleep/wake conditions involving different combinations of TSD (40 to 88 h), CSR (2 to 6 h of sleep/night), control (8 to 10 h of sleep/night), and nap (nocturnal and diurnal) schedules.

   Subsequently, we used the UMP to simulate different sleep/wake schedules to address three additional research questions:
2. Can we determine the number of recovery nights and the associated recovery time in bed (TIB)/night

Table 1—Sleep/wake schedules of the six different sleep studies (from four different laboratories) used in our analyses.

Study	Study Condition # (n)	Sleep/Wake Schedule (w_i)			Wake Time (h)
		Baseline	TSD/CSR/Control	Recovery	
Training (T)					
T1[6]	1 (14)	3 nights, 8 h TIB	7 nights, 3 h TIB	3 nights, 8 h TIB	07:00
	2 (12)	"	7 nights, 5 h TIB	"	"
	3 (15)	"	7 nights, 7 h TIB	"	"
	4 (16)	"	7 nights, 9 h TIB	"	"
Validation (V)					
[a]V1[8]	5 (19)	7 nights, 10 h TIB	64 h TSD	3 nights, 8 h TIB	07:00
	6 (19)	"	7 nights, 3 h TIB	"	"
V2[10]	7 (12)	2 nights, 10 h TIB	62 h TSD	2 nights, 10 h TIB	08:00
	8 (11)	"	2 nights, 10 h TIB	"	"
[a]V3[11]	9 (18)	1 night, 8 h TIB	40 h TSD	1 night, 8 h TIB	07:00
	10 (18)	"	5 nights, 4 h TIB	"	"
V4[12]	11 (13)	2 nights, 10 h TIB	5 nights, 4 h TIB	1 night, 0 h TIB	08:00
	12 (27)	"	"	1 night, 2 h TIB	"
	13 (29)	"	"	1 night, 4 h TIB	"
	14 (25)	"	"	1 night, 6 h TIB	"
	15 (21)	"	"	1 night, 8 h TIB	"
	16 (27)	"	"	1 night, 10 h TIB	"
V5[14]	17 (13)	3 nights, 8 h TIB	88 h TSD	3 nights, 8 h TIB	07:30
	18 (12)	"	88 h, 2-h naps (one every 12 h)	"	"[b]

[a]Crossover design. [b]Wake times for the 2-h naps were 04:45 and 16:45. CSR, chronic sleep restriction; TIB, time in bed; TSD, total sleep deprivation.

required to return neurobehavioral performance to a given basal level observed prior to sleep loss?

3. Can we quantify the neurobehavioral performance benefit derived from sleep extensions (e.g., 10 h TIB/night versus 8 h TIB/night) prior to sleep loss?
4. Can we assess the differential neurobehavioral impact of a split-sleep schedule versus a consolidated sleep schedule?

METHODS

Datasets

We obtained psychomotor vigilance task (PVT) lapse data (number of response times > 500 msec) or simple reaction-time test (SRTT) lapse data from six different previously published sleep studies conducted in four different laboratories, reflecting a total of 18 different sleep/wake conditions. The SRTT is a reaction-time test similar to the PVT; the only difference was that the visual stimulus used in the former is a black square displayed on a screen at randomized (2–7 sec) intervals over 10 min, whereas in the latter it is a running counter displayed on a screen at randomized (2–10 sec) intervals.[9] We then used data from one of these studies (*Study T1*) for estimating the UMP model parameters, and data from the remaining five studies (*Studies V1–V5*) for validating the model predictions. Table 1 summarizes the sleep/wake conditions [consisting of baseline, TSD/CSR/control, and recovery phases] for each of the six studies, which are briefly described next.

Study T1[6]

Fifty-seven healthy adults (ages 24–62 y, mean 38 y) underwent 7 consecutive nights of 3, 5, 7, or 9 h TIB (CSR phase) followed by 3 consecutive nights of 8 h TIB (recovery phase) in a controlled laboratory study. A 10-min PVT was administered four times per day (09:00, 12:00, 15:00, and 21:00). Subjects in the 3- and 5-h TIB study conditions performed additional PVT sessions (at 00:00 for both study conditions and again at 02:00 for the 3-h TIB study condition) during their additional time awake.

Study V1[8]

Nineteen healthy adults (ages 18–39 y, mean 28 y) underwent two sleep-loss challenges (crossover design) separated by 2–4 w: (1) 64 h TSD and (2) CSR consisting of 7 consecutive nights of 3 h TIB. During the entire wake period of TSD and CSR, 10-min PVTs were administered every 2 h.

Study V2[10]

Twenty-three healthy adults (ages 22–38 y) were randomly assigned to either a 62-h TSD or a control schedule of 10 h TIB for 2 consecutive nights. A 10-min PVT was administered every 2 h throughout most of the time awake. (Mean age of the participating subjects was not reported in the original publication.[10])

Study V3[11]

Eighteen healthy middle-aged volunteers (ages 46–55 y, mean 50 y) underwent two sleep-loss challenges (crossover design)

separated by at least 2 w: (1) 40 h TSD and (2) CSR consisting of 5 consecutive nights of 4 h TIB. Subjects performed a 10-min SRTT every 2 h from 08:00 to 22:00 on each day. Only daily averaged values of transformed lapses ($\sqrt{lapses}$ + $\sqrt{lapses + 1}$) were reported for this study.[11]

Study V4[12,13]

Following CSR of 5 consecutive nights of 4 h TIB, 142 healthy adults (ages 22–45 y, median 29 y) were randomly assigned to one of the following six recovery sleep schedules: 1 night of 0, 2, 4, 6, 8, or 10 h TIB. A 10-min PVT was administered every 2 h throughout the wake periods. (Note: Although the 0-, 2-, 4-, 6-h TIB nights cannot be generally considered as "recovery," we use this terminology to maintain consistency across all the other studies.)

Study V5[14–16]

Twenty-five healthy adults (ages 21–48 y, mean 28 y) were randomly assigned to one of the following two schedules during 88 h of TSD: (1) no naps or (2) 2-h naps every 12 h. A 10-min PVT was administered every 2 h throughout most of the time awake.

Unified Model of Performance

Achermann and Borbely's[17] two-process model postulates that the temporal pattern of performance can be represented as the additive interaction of two processes. The first, process *S*, represents the homeostatic influence on performance wherein the homeostat increases during wake and decreases during sleep. In the original two-process model, these increases/decreases operate within fixed upper and lower asymptotes that are independent of prior sleep debt. The second process is the endogenous circadian rhythm, process *C*, which is independent of the sleep/wake history and represents a self-sustaining oscillator with a 24-h period.[17]

The UMP[5,18] was developed as an extension of the original two-process model. In the UMP, process *S* is dependent on prior sleep debt such that the capacity to recover during sleep varies inversely with extant sleep debt. Specifically, the UMP modulates the lower asymptote of process *S* as a function of the sleep debt resulting from prior sleep/wake history such that the most recent sleep loss exerts the greatest effect, with the sleep loss influence decreasing with increasing temporal distance. Table 2 summarizes the biomathematical equations (Equations 1–5) governing the UMP, where Equations 2–3 describe processes *C* and *S*, respectively, Equation 4 describes the effect of sleep debt on the lower asymptote of process *S*, and Equation 5 describes the accumulation and restoration of sleep debt as a function of the sleep/wake history.

The UMP consists of eight parameters: (1) U, the upper asymptote of the homeostatic process *S*; (2) τ_w, the time constant of increasing homeostatic pressure during wake time; (3) τ_s, the time constant of decreasing homeostatic pressure during sleep; (4) S_0, the initial state value for process *S*; (5) κ, the amplitude of the circadian process *C*; (6) φ, the circadian phase; (7) τ_{LA}, the time constant accounting for the exponential rise and fall of sleep debt (via modulation of the lower asymptote L) as a function of sleep/wake history; and (8) L_0, the initial state value of L. The first six parameters originate from the original two-process model, whereas the last two parameters account for the effects of sleep debt.

In this work, we modified the UMP to more accurately quantify the effect of sleep debt on process *S*. The original UMP[5] quantifies the sleep debt to lie within a range of −2 and 1, where −2 corresponds to the asymptotically approached lower debt limit associated with 24 h of sleep/day, and 1 corresponds to the asymptotic upper debt limit associated with total sleep loss (0 h sleep/day). However, it is unlikely that normal, healthy, non-sleep-deprived individuals can sleep for 24 consecutive hours during 24 h of TIB. In fact, the estimated maximal capacity for sleep (under well-rested conditions) in young adults when given 16 h of sleep opportunity per 24 h is 8.9 h.[19] Therefore, in the current work, we modified the UMP to impose a minimum debt level of −0.11 (corresponding to the asymptotic debt limit associated with 8.9 h of sleep/day) instead of the previous limit of −2. (The revised debt limit associated with 8.9 h of sleep/day is reached only under well-rested conditions. Under sleep-deprived conditions or when carrying a positive sleep debt, an individual can certainly sleep > 8.9 h/day, and this is considered in our model.)

Estimation of UMP Parameters

To obtain the UMP parameters using data from *Study T1*, we minimized the combined sum of the squared errors between the model outputs and the PVT lapse data from the four different study conditions 1–4 in the study (see Table 1). Specifically, we minimized the following objective function to obtain the eight UMP parameters $\Theta = (U, \tau_w, \tau_s, S_0, \kappa, \varphi, \tau_{LA}, L_0)$:

$$J(\Theta) = \sum_{i=1}^{4} \sum_{t=1}^{T_i} \left[\overline{P}_m^i(t) - P(t, w_i, \Theta) \right]^2 \qquad (6)$$

where $\overline{P}_m^i(t)$ denotes the group-average data from the *i*-th study condition at time t, T_i denotes the total number of measurements available in the *i*-th study condition, w_i denotes the sleep/wake schedule of the *i*-th study condition, and $P(t, w_i, \Theta)$ denotes the UMP output at time t corresponding to w_i and Θ.

For *Study T1*, S_0 and L_0 represented the S and L values at the beginning of the baseline phase. However, because S_0 and L_0 are parameters that depend on the prior sleep/wake history and because in each of the validation studies *V1–V5* subjects slept for ~8 h for at least 3 d prior to the study,[8,10–12,14] for the validation studies, we computed the S and L values corresponding to the end of the baseline of *Study T1* (3 d of 8 h TIB) and assigned them as the S_0 and L_0 for all study conditions. Specifically, the S_0 and L_0 parameters were computed to be 0.50 and 0.00 lapses, respectively.

UMP Predictions

A review of the inclusion/exclusion criteria for *Studies V1–V5* revealed that subjects were similar to those in *Study T1* in terms of sleep habits, caffeine use, etc. Accordingly, we assumed that the entrained circadian phase φ of each group of subjects was similar across all studies. We then computed the performance predictions (i.e., PVT or SRTT lapses) for each of the conditions in the validation studies as $P(t, w_i, \Theta)$, where w_i was obtained from Table 1.

Table 2—Governing equations of the unified model of performance (UMP).

Performance impairment (P):

$$P(t) = S(t) + \kappa C(t) \quad (1)$$

where C and S denote the circadian and homeostatic processes of the two-process model at time t, respectively, and κ represents the circadian amplitude.

Circadian process (C):

$$C(t) = \sum_{i=1}^{5} a_i \sin\left[i \frac{2\pi}{\tau}(t + \varphi)\right] \quad (2)$$

where a_i, i = 1, ..., 5, represent the amplitude of the five harmonics (a_1 = 0.97, a_2 = 0.22, a_3 = 0.07, a_4 = 0.03, and a_5 = 0.001), τ denotes the period of the circadian oscillator (~24 h), and φ denotes the circadian phase.

Homeostatic process (S):

$$\frac{dS(t)}{dt} = \begin{cases} [U - S(t)]/\tau_w & \text{during wakefulness} \\ [L(t) - S(t)]/\tau_s & \text{during sleep} \end{cases} \quad (3)$$

where U and L denote the upper and lower asymptotes of process S, respectively, τ_w and τ_s denote the time constants of the increasing and decreasing sleep pressure during wakefulness and sleep, respectively. $S(0) = S_0$ and $L(0) = L_0$ correspond to the initial state values for S and L, respectively. (See text)

Lower asymptote (L) of process S:

$$L(t) = U \times Debt(t) \quad (4)$$

where $Debt$ denotes the sleep debt.

Sleep debt ($Debt$):

$$\frac{dDebt(t)}{dt} = [Loss(t) - Debt(t)]/\tau_{LA} \quad (5a)$$

$$Loss\ (t) = \begin{cases} 1 & \text{during wakefulness} \\ -2 & \text{during sleep} \end{cases} \quad (5b)$$

where τ_{LA} denotes the time constant of the exponential decay of the effect of sleep history on performance.

Refer to Rajdev et al.[5] for additional details.

In the datasets considered in this work, we observed that the PVT and SRTT performance differed on the first day of TSD/CSR across studies, despite having the same sleep/wake schedules during the baseline phase. This could be due to various reasons, such as differences in the actual time asleep for a given TIB, between-study differences in the workload of the experimental protocols (e.g., frequency of PVTs, number and frequency of other performance tests, etc.), differential effects of seasonal variations in moods on subjects' performances, and differences between sleep laboratories (and the conditions within them). To account for these differences, and effectively normalize performance data across the study conditions, we added a constant value δ to the UMP predicted output $P(t, w_i, \Theta)$ for each study condition, where δ was computed as the difference between the average number of measured PVT (or SRTT) lapses and the average number of predicted lapses $P(t, w_i, \Theta)$ on the first day of TSD/CSR for that particular study condition.

Goodness of Fit

To assess the goodness of fit (on data from *Study T1*) and predictions (on data from *Studies V1–V5*), we calculated the root mean squared errors (RMSEs) between the UMP model outputs $P(t, w_i, \Theta)$ (fits and predictions) and the group-average PVT or SRTT lapse performance data for each study condition.

To provide an alternate goodness of fit for the UMP predictions, we quantified the likelihood that the predictions came from the same distribution as the group-average data. Specifically, we computed the percentage of model predicted points that lie within a 95% confidence interval (CI) of the group-average data, wherein we used the standard errors of the data to compute the CIs (95% CI ≈ 2 standard errors).[20] Thus, higher percentage values indicate greater likelihood and, hence, better predictions. Such a metric is justified because if the model prediction at a particular time instant is considered as another "measurement" of group-average performance, it would be

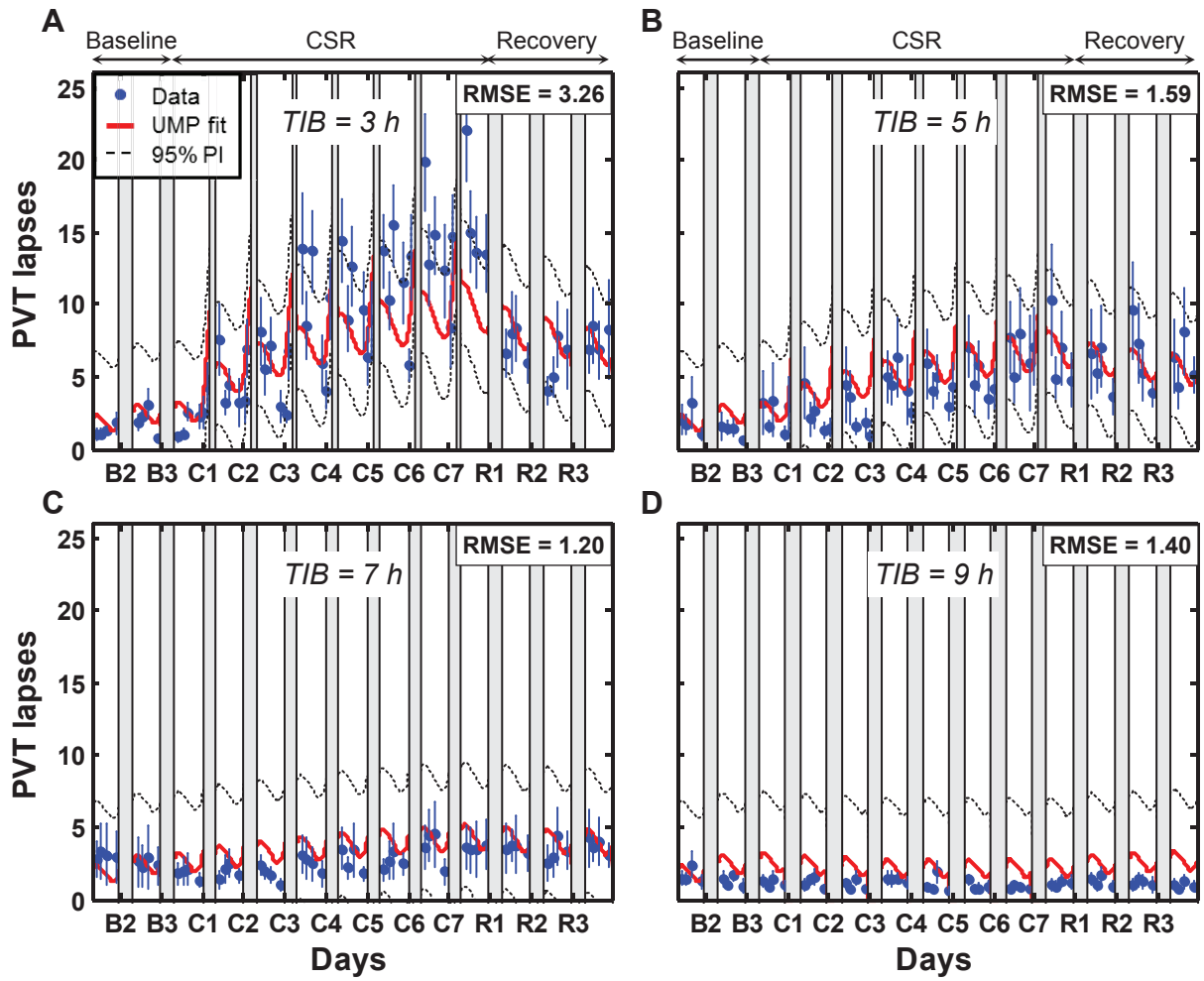

Figure 1—Group-averaged lapse data (standard errors) and unified model of performance (UMP) fits on baseline (B2–B3), chronic sleep restriction (CSR; C1–C7), and recovery (R1–R3) phases in *Study T1*.[6] The four panels A-D correspond to the 3-, 5-, 7-, and 9-h time in bed (TIB) study conditions (1–4; Table 1) in *Study T1*, respectively. Gray-shaded vertical bars represent sleep episodes. Also shown are root mean squared errors (RMSE; lapses) between measured data and UMP fits, and 95% prediction intervals (PI) of the model outputs (dashed black lines).

expected to lie within the 95% CI of the group-average data at that time instant.

RESULTS

Estimated UMP Parameters and Fits on Study T1

By minimizing the objective function in Equation 6, we obtained the following UMP parameter estimates (standard error): U = 18.35 (0.73) lapses, τ_w = 40.00 (3.19) h, τ_s = 2.11 (0.11) h, S_0 = 0.00 (0.66) lapses, κ = 3.26 (0.26) lapses, φ = 2.31 (0.26) h, τ_{LA} = 7.00 (1.67) d, L_0 = −4.96 (0.00) lapses. Figure 1A–1D shows the corresponding fits on data from each of the four study conditions (one in each panel) in *Study T1*. The UMP was able to capture the dose-dependent effect of TIB on performance during CSR, yielding RMSEs ranging from 1.20 lapses (for the 7-h TIB condition) to 3.26 lapses (for the 3-h TIB condition). Although the fit on the last 2 d of CSR for the 3-h TIB condition was, on average, lower than the data by 4.92 lapses, it successfully captured the slower recovery in this study condition (with an average discrepancy of only 0.86 lapses) in comparison to the recovery times in the other study conditions.

Validation of UMP Predictions on Studies V1–V5

We used the UMP parameters (as obtained from *Study T1*) to predict performance in the 14 different sleep/wake conditions of *Studies V1–V5* in Table 1. We then validated the UMP predictions by comparing against the measured data for each of the 14 study conditions.

Figure 2 shows performance data and UMP predictions during the TSD/CSR and recovery phases of *Study V1* (study conditions 5 and 6 in Table 1). Except for the PVT sessions between T1 and T2 (TSD challenge) and the first sessions immediately following sleep between C4 and C7 (CSR challenge), the UMP accurately predicted the effects of sleep loss during both TSD and CSR (and the recovery phases following them), yielding overall RMSEs of 2.46 and 2.39 lapses, respectively. Also, for TSD and CSR, 80% and 76% of the model predictions fell within the 95% CIs of the measured data, respectively. As

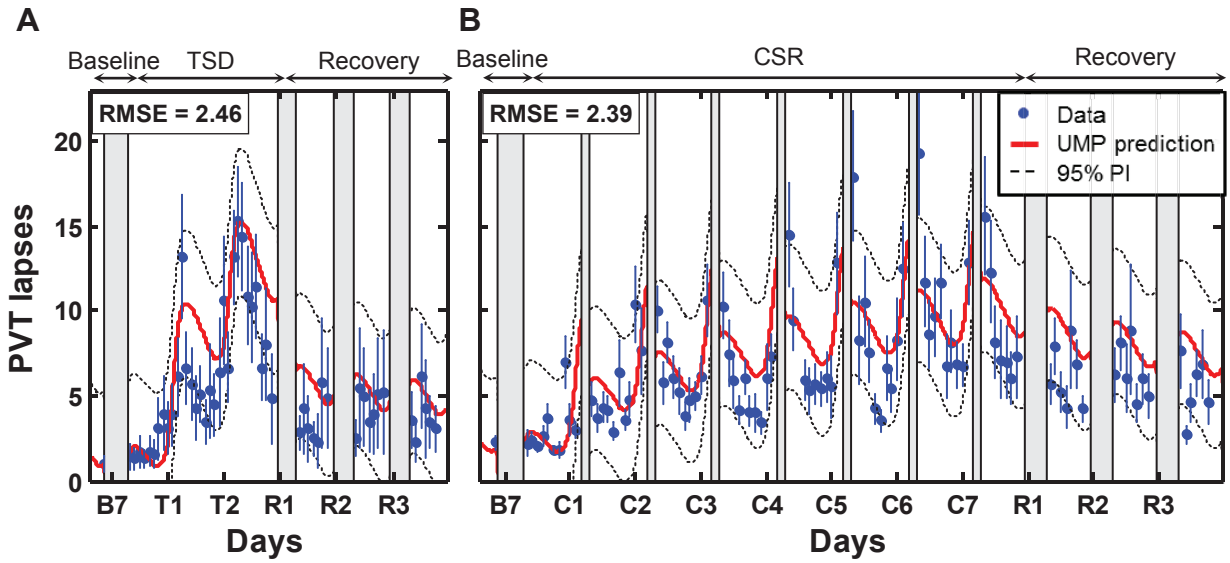

Figure 2—Group-averaged lapse data (standard errors) and unified model of performance (UMP) predictions on baseline (B7), total sleep deprivation (TSD; T1–T2)/chronic sleep restriction (CSR; C1–C7), and recovery (R1–R3) phases in *Study V1*.[8] Panels A and B correspond to the 64-h TSD and 3-h time in bed CSR study conditions (5–6; Table 1) in *Study V1*, respectively. Gray-shaded vertical bars represent sleep episodes. Also shown are root mean squared errors (RMSE; lapses) between measured data and UMP predictions, and 95% prediction intervals (PI) of the model outputs (dashed black lines).

observed in the data, the UMP also predicted a faster recovery following 64 h TSD compared to CSR of 7 nights of 3 h TIB.

Figure 3 illustrates performance data and UMP predictions for *Study V2* (study conditions 7 and 8 in Table 1). For study condition 7 (TSD), the UMP accurately predicted lapses during baseline, the initial portion of the TSD phase, and the recovery phase. However, it underpredicted lapses during the latter part of the TSD phase, yielding an overall RMSE of 3.80 lapses (Figure 3A). Nevertheless, 79% of the lapse predictions fell within the 95% CIs of the data. For study condition 8 (control; no sleep loss), the UMP accurately predicted lapses across all phases, yielding an RMSE of 1.13 lapses, with 100% of the predictions lying within the 95% CIs of the data.

Figure 4 shows performance data and UMP predictions for *Study V3* (study conditions 9 and 10 in Table 1). For this study, SRTT lapse data were transformed ($\sqrt{lapses} + \sqrt{lapses + 1}$) and daily means were reported. Accordingly, we transformed the UMP predictions and plotted them as a single daily average in Figure 4. Qualitatively, the UMP predictions accurately tracked performance trends during both TSD (Figure 4A) and CSR (Figure 4B) phases except for day C5 during CSR, where the measured data show an unexpected improvement in performance from day C4 to day C5. Quantitatively, the RMSEs (based on daily means) were 0.63 and 0.50 transformed lapses for the TSD and CSR conditions, respectively. The largest prediction error observed on day T1 during TSD (Figure 4A) was ~1 transformed lapse, which corresponds to ~3 non-transformed lapses. For both conditions, 100% of the predictions were within the 95% CIs of the data.

Figure 5 illustrates performance data and UMP predictions for *Study V4* (study conditions 11–16 in Table 1). The UMP accurately predicted performance during CSR days C1–C4 and slightly underpredicted lapses on day C5, yielding an RMSE of 1.77 lapses across the baseline and CSR phases (Figure 5A). In the original publication, standard errors of the data during the baseline and CSR phases were not provided; consequently, the percentage of predictions falling within the 95% CIs of the data could not be computed. Also, the data obtained during the recovery phases were reported only as daily averaged lapses. Therefore, we plotted the daily averaged UMP predictions for the six different recovery phases (Figure 5B–5G). This, however, precluded calculation of RMSEs for the various recovery phases. However, 83% of the daily averaged predictions were within 95% CIs of the daily averaged data. Overall, the UMP successfully predicted the dose-dependent effect of TIB during recovery. For the 8-h TIB/night recovery phase, UMP-predicted lapses were indistinguishable from the measured performance data (Figure 5F). The UMP underpredicted lapses in the 0-, 2-, and 4-h TIB/night recovery phases, and slightly overpredicted lapses in the 6- and 10-h TIB/night recovery phases. With the exception of the 0-h TIB/night recovery phase, discrepancies between UMP predictions and measured data were less than 3 lapses.

Figure 6 illustrates performance data and UMP predictions for *Study V5* (study conditions 17 and 18 in Table 1). For the 88-h TSD condition (Figure 6A), the UMP generally underpredicted lapses for the most part, yielding an overall RMSE of 4.16 lapses. However, the measured data exhibited large standard errors and more than 75% of the UMP group-average predictions fell within the 95% CIs of the data. In contrast, the UMP predictions were quite accurate (RMSE = 2.07 lapses) for the 2-h nap condition illustrated in Figure 6B, with more than 90% of the predictions falling within the 95% CIs of the data.

UMP Predictions for Simulated Sleep/Wake Scenarios

After validating the UMP predictions, we used the model to investigate (via simulations): (1) the number of nights and TIB/

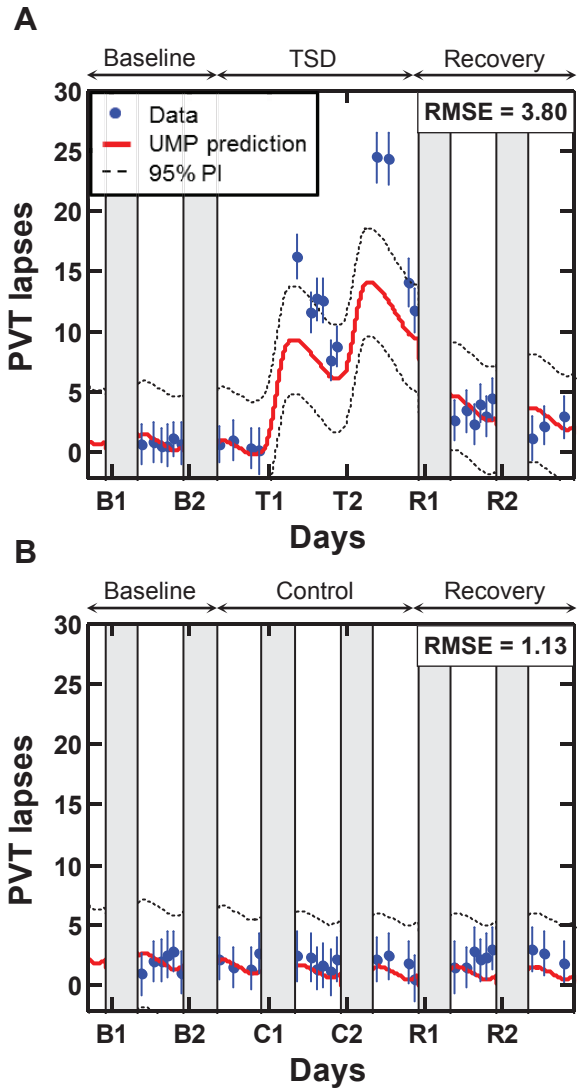

Figure 3—Group-averaged lapse data (standard errors) and unified model of performance (UMP) predictions on baseline (B1–B2), total sleep deprivation (TSD; T1–T2)/control (C1–C2), and recovery (R1–R2) phases in *Study V2*.[10] Panels A and B correspond to the 62-h TSD and 10-h time in bed control study conditions (7–8; Table 1) in *Study V2*, respectively. Other descriptors are identical to those in Figure 2.

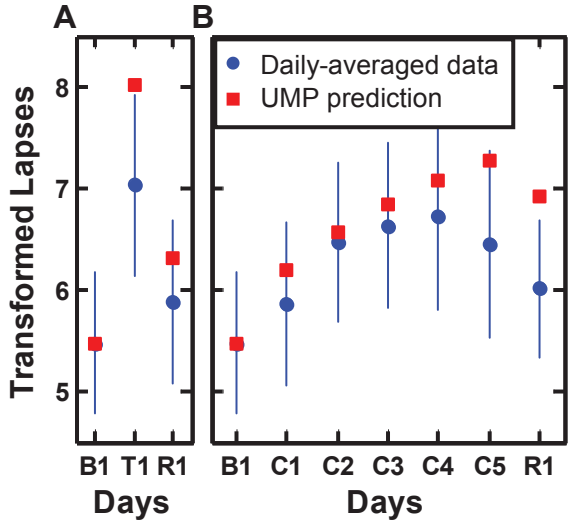

Figure 4—Group-averaged transformed lapse ($\sqrt{lapses} + \sqrt{lapses + 1}$) data (standard errors) and unified model of performance (UMP) predictions averaged over each day on baseline (B1), total sleep deprivation (T1)/chronic sleep restriction (C1–C5), and recovery (R1) phases in *Study V3*.[11] Panels A and B correspond to the 40-h TSD and 4-h time in bed CSR study conditions (9–10; Table 1) in *Study V3*, respectively.

night required for complete recovery (i.e., return to the basal performance level observed under habitual 8 h TIB/night) following 64 h TSD and 7 nights of 3 h TIB (*Study V1*); (2) the effect of prior sleep history on performance during TSD/CSR and during recovery in *Study V1*; and (3) the effect of split-sleep schedule versus consolidated sleep on performance in *Study V5* (study condition 18 in Table 1).

Number of nights and TIB per night for complete recovery

We used the UMP to generate performance predictions under the following two alternative *recovery* scenarios for TSD and CSR conditions in *Study V1*: (1) 10 nights of 8 h TIB and (2) 10 nights of 10 h TIB. We then defined complete recovery as maintenance of PVT lapses within 20% of the maximum basal performance level across an entire recovery day. Here, basal performance was defined as the number of predicted lapses between 07:00 and 23:00 on the last day of 8 h TIB/night (of 7 nights) preceding the first 10-h TIB baseline night (*Study V1*).

Figure 7 illustrates the UMP-predicted performance under these two recovery scenarios for TSD (Figure 7A) and CSR (Figure 7B). For the TSD condition, the UMP predicted that complete recovery would occur after the 3rd night of 10-h TIB scenario. In contrast, complete recovery would occur only after 10 nights with 8 h nightly TIB. For the CSR condition, the UMP predicted that complete recovery would occur after the 5th night of 10-h TIB scenario; however, it would not be achieved even after 10 nights of 8 h nightly TIB. (The UMP predicted that complete recovery would require 14 nights of 8 h nightly TIB.) These results suggest that only 2 h of additional sleep can significantly speed up recovery following sleep loss. Indeed, these findings are in line with the observations of Faraut et al.,[21] who noted that following a night of acute sleep restriction (2 h of sleep for 1 night), young healthy adults are able to return to normal baseline levels of alertness by extending the duration of the recovery night from 8 h to 10 h.

Effect of prior sleep history

In *Study V1*, subjects were subjected to 10 h TIB for 7 consecutive nights prior to the TSD/CSR phase (see Table 1). To determine the effect of *prior sleep history* on performance, we simulated and compared the effects of 7 consecutive nights of 10 h TIB (original study design) with those of 7 consecutive nights of 7 h TIB on subsequent performance during TSD/CSR and recovery (the latter consisting of 8 h TIB/night, as per the original study). Figure 8 illustrates the UMP-predicted performance under these two prior sleep history scenarios for TSD/recovery (Figure 8A) and CSR/

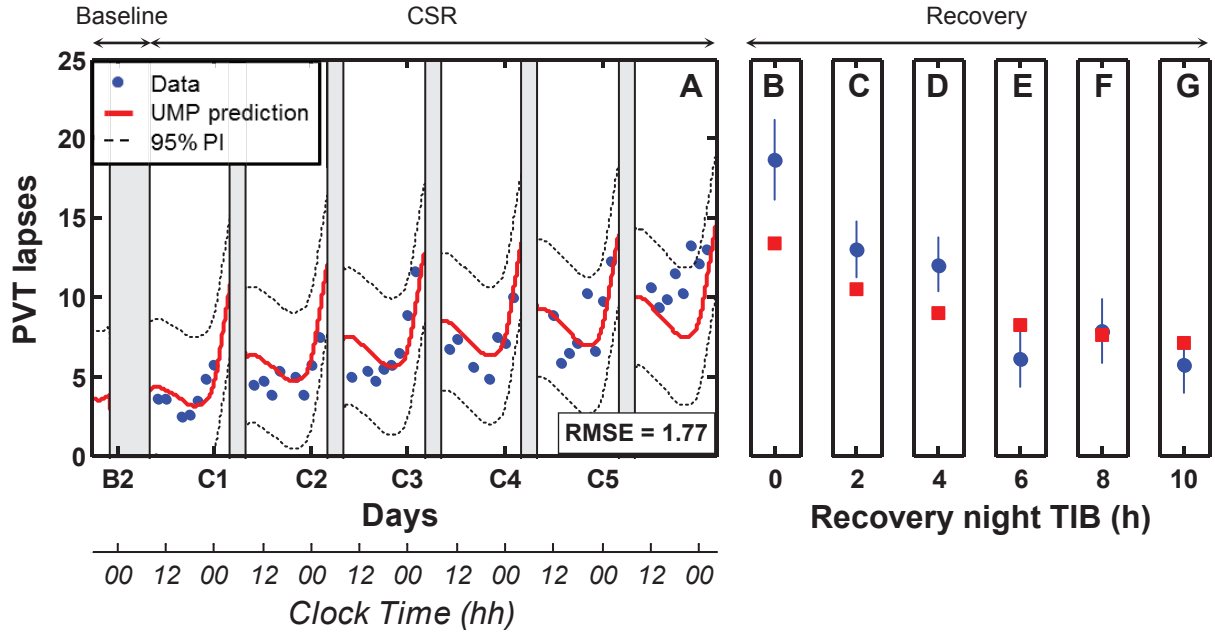

Figure 5—Group-averaged lapse data and unified model of performance (UMP) predictions on baseline (B2), chronic sleep restriction (CSR; C1–C5), and six different recovery time in bed (TIB) phases in *Study V4*.[12] Panel A shows the measured data (averaged across all 142 subjects in the six study conditions 11–16; Table 1) and the UMP prediction for the baseline and CSR phases. Panels B–G show daily-averaged measured data (standard errors) and UMP predictions during recovery night of 0, 2, 4, 6, 8, and 10 h TIB (study conditions 11–16; Table 1), respectively. Other descriptors are identical to those in Figure 2. (Standard errors of the measured data were not available for the baseline and CSR phases.)

recovery (Figure 8B). As expected, the UMP predicted that performance during TSD/recovery would be better following 7 nights of 10 h TIB than following the 7 nights of 7-h TIB scenario. However, it predicted that the performance benefits of extended TIB would gradually fade away across the TSD days (from 3.29 to 0.66 lapses) and the recovery days (from 1.75 to 0.33 lapses). For the 10-h TIB scenario, the UMP predicted that complete recovery would be reached after the 10th night. For the 7-h TIB scenario, it predicted that complete recovery would be reached only after 14 nights of 8 h nightly TIB; however, the predicted benefit of the 10-h TIB scenario over the 7-h TIB scenario was less than one lapse after 5 recovery nights. For the CSR/recovery condition, the UMP predicted that performance benefits derived from 7 prior nights of 10 h TIB would decrease across the CSR days (from 3.29 to 0.61 lapses) and the recovery days (from 0.86 to 0.16 lapses). In addition, during recovery, neither prior sleep history scenario would reach complete recovery by the 10th day. The UMP predicted that complete recovery would require 14 nights of 8 h nightly TIB for the 10-h TIB scenario and 15 nights of 8 h nightly TIB for the 7-h TIB scenario; however, the predicted benefit of the 10-h TIB scenario was less than one lapse during the recovery days. Overall, the model predicted that the effect of prior sleep history on performance would fade away with increasing days of either form of sleep loss, but would became prevalent again, albeit to a lesser extent, during the first few recovery days. These predictions are in concurrence with results reported by Rupp et al.,[7] where extending sleep prior to CSR slows performance degradation and provides faster subsequent recovery.

Effect of a split-sleep schedule over consolidated sleep

In the nap condition of *Study V5* (study condition 18 in Table 1), subjects took 2-h naps every 12 h during 88 h of sustained wakefulness (Figure 6B). This sleep/wake schedule can be considered as a form of split-sleep schedule with 4 h TIB per day. To determine the effect of such a split-sleep schedule versus consolidated sleep of 4 h TIB (nocturnal or diurnal), we generated UMP predictions for the following two conditions: 4 h nocturnal sleep (01:45 to 05:45) and 4 h diurnal sleep (13:45 to 17:45). Figure 9 illustrates the UMP predictions under the split-sleep schedule and the two consolidated sleep conditions. Under each condition, the UMP predicted that performance would be the worst during the early part of the day (06:00–11:00) and the best during the early evening hours of the day (18:00–23:00). The model predicted that performance under the split-sleep schedule would lie in between the performance trajectories observed under the two consolidated sleep conditions. Specifically, in the morning hours, performance under the split-sleep schedule would be much better than consolidated diurnal sleep, and slightly worse (less than one lapse) than consolidated nocturnal sleep. In the evening hours, it would be much better than consolidated nocturnal sleep and slightly worse (less than two lapses) than consolidated diurnal sleep. Thus, overall, the split-sleep schedule would provide a better compromise than either of the two consolidated 4 h TIB/day conditions. More importantly, splitting up sleep would not negatively affect daytime performance compared to a consolidated sleep period of the same total duration, which is supported by a couple of prior studies.[22,23]

DISCUSSION

To be useful, a model needs to accurately predict neurobehavioral performance across conditions and subjects not used to develop the model. Hence, our first goal was to validate the UMP on PVT performance data from five studies that encompassed a wide range of sleep/wake schedules, including ones considerably different from those used in model development. After validation, we demonstrated how the UMP can be used to generate testable hypotheses on the effects of specific sleep/wake schedules on PVT performance. In particular, we simulated different schedules to assess the effect of the number of nights (and TIB per night) required for complete recovery following sleep loss, the beneficial effect of sleep extension prior to sleep loss, and the effect of split-sleep schedule *vis-à-vis* consolidated sleep.

Our first objective was to determine the extent to which the UMP developed using data from one study (composed of four different CSR conditions involving 7 d of 3, 5, 7, and 9 h TIB/night) accurately predicted performance data from five different studies comprising a total of 14 different sleep/wake conditions. These five studies, conducted in four different laboratories, included different combinations of TSD (40 to 88 h), CSR (2 to 6 h TIB/night), control (8 to 10 h TIB/night), and nap (nocturnal and diurnal) schedules. Overall, across all studies, the UMP accurately predicted the performance trends during each of the sleep/wake schedules. Quantitatively, the UMP prediction accuracy was high, with RMSEs across studies ranging from 7% to 36% of the maximum impairment levels. Importantly, on average, 87% of the UMP predictions lay within 2 standard errors of the measured data, which ranged from 14% to 117% of the maximum impairment levels. In general, the prediction accuracy was higher for the conditions that included partial sleep loss versus the no-sleep (TSD) conditions. It is not clear if this should be attributed to the fact that the model was developed using CSR data or because TSD is, in fact, harder to predict. For conditions that included partial sleep loss, the measured data invariably fell within the 95% prediction intervals of UMP-predicted values. In addition, consistent with prior findings that humans exhibit trait-like responses to sleep loss, the accuracy of the UMP predictions was more homogenous in crossover design studies (*Studies V1* and *V3*)[8,11] than in parallel-group design studies (*Studies V2*, *V4*, and *V5*).[10,12,14]

Qualitatively, the UMP accurately captured the temporal dynamics of performance in all study conditions investigated in this work, yielding an average Pearson correlation coefficient of 0.86. However, quantitatively, it tended to underpredict lapses, particularly after extended sleep loss or during periods of increased extant sleep debt (e.g., Figures 3A, 5B, and 6A), except for two study conditions involving 64 h TSD and 7 nights of 3-h TIB CSR[8] (Figure 2). Lapse underpredictions could be due to many reasons. First, the model-generated predictions were based on the presumption that TIB was equivalent to time asleep. However, TIB represents an overestimation of actual sleep obtained under conditions in which sleep efficiency is reduced, most notably during extended sleep periods.[7] Furthermore, most of the studies modeled here did not report actual sleep or TIB during the pre-baseline phase, which therefore could have been greater or less than the assumed 8 h. Second,

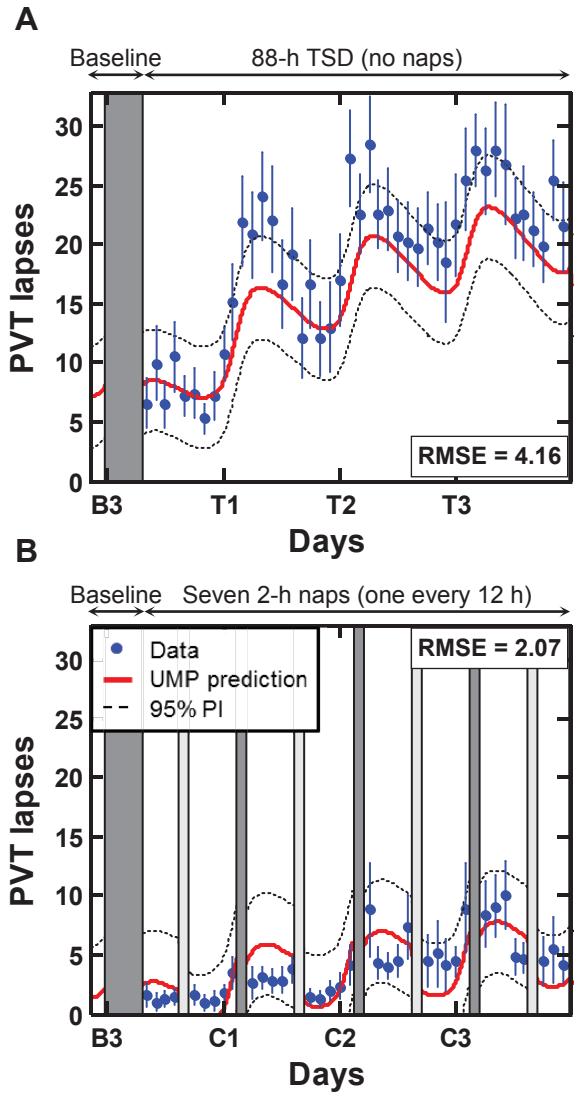

Figure 6—Group-averaged lapse data (standard errors) and unified model of performance (UMP) predictions on baseline (B3), no naps (T1–T3), and 2-h naps every 12 h (C1–C3) phases in *Study V5*.[14] Panels A and B correspond to the 88-h TSD and 2-h naps study conditions (17–18; Table 1) in *Study V5*, respectively. The dark- and light-gray shaded vertical bars represent the nocturnal and diurnal sleep episodes, respectively. Other descriptors are identical to those in Figure 2.

in the UMP, the recovery capacity during sleep varies as a function of extant sleep debt (i.e., the lower asymptote L of the homeostatic process increases or decreases with increasing or decreasing sleep debt, respectively, while the upper asymptote U is held constant).[5] However, it is possible that the maximum performance degradation during wake time, which is represented by U, is also a monotonic function of sleep debt, which then could account for the increased lapses observed during extended sleep loss. Data from additional extended sleep-loss studies would, however, be needed to determine the appropriate enhancements to the UMP.

The UMP overpredicted lapses in one study involving 40 h of TSD and 5 nights of 4-h TIB CSR study conditions (Figure 4). We speculate that this may be because the subjects involved in

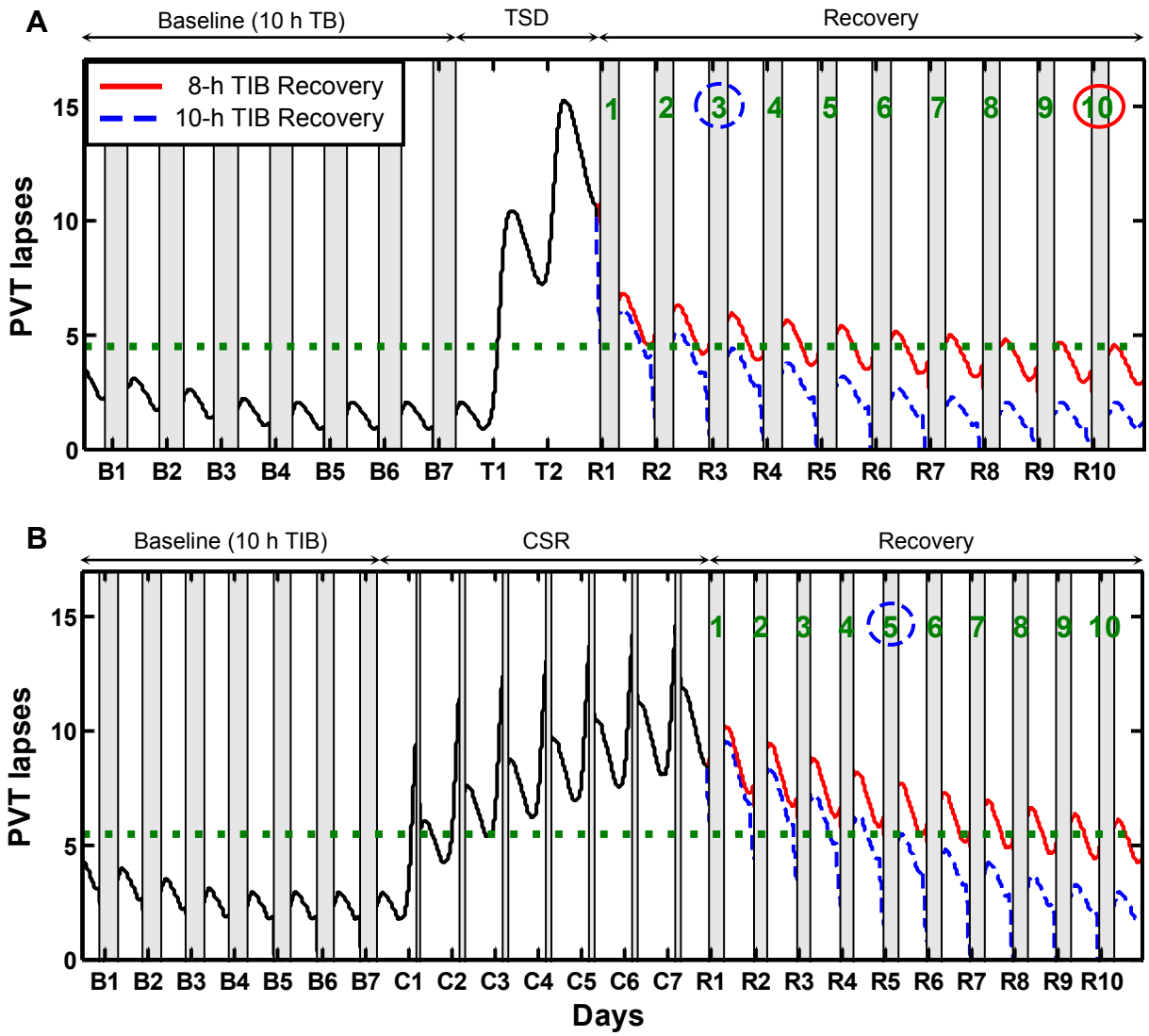

Figure 7—Unified model of performance (UMP) simulations for baseline (B1–B7), total sleep deprivation (TSD; T1–T2)/chronic sleep restriction (CSR; C1–C7), and recovery (R1–R10) phases under two different recovery scenarios for *Study V1*.[8] Panels A and B correspond to the 64-h TSD and 3-h time in bed (TIB) CSR study conditions (5–6; Table 1), respectively. Black solid lines represent the UMP predictions up to the first recovery night. Solid red and dashed blue lines represent UMP predictions during the recovery nights for the 8- and 10-h TIB recovery scenarios, respectively. The dotted green horizontal line corresponds to the threshold used to define complete recovery (within 20% of the maximum basal performance level). Gray-shaded vertical bars represent the sleep episodes. Also indicated, within red and dashed blue circles, are the number of recovery nights required for complete recovery under the 8- and 10-h TIB recovery scenarios, respectively.

this study were middle-aged (46–55 y) with a mean age of 50 y; the mean ages of subjects in all the other studies ranged from 28 to 38 y. In comparison with young subjects, healthy adults of older ages typically feel less sleepy after sleep deprivation, and they show fewer response lapses on the PVT.[24] Because the UMP was developed using lapse data from relatively younger subjects, it might tend to overpredict lapses for older subjects. Therefore, future modeling efforts might have to account for the effects of age on neurobehavioral performance.

Our second and third objectives were to demonstrate the use of UMP in (1) determining the number of recovery nights (and the associated TIB/night) required for complete recovery following sleep loss and (2) quantifying the beneficial effect of sleep extension prior to sleep loss. UMP simulations of two different recovery scenarios following 64 h of TSD and 7 consecutive nights of 3-h TIB CSR (Figure 7) suggested that only 2 h of additional recovery sleep can significantly speed up recovery following sleep loss from 10 to 3 nights for TSD and from 14 to 5 nights for CSR. Similarly, simulations of two different baseline conditions (Figure 8; 7 consecutive nights of 10-h TIB and 7 consecutive nights of 7-h TIB) preceding TSD and CSR suggested that prior sleep extension (10-h TIB/night) is beneficial, improving performance by at least three lapses during sleep loss (and, to a lesser extent, during subsequent recovery). The simulations also suggested that the effect of prior sleep history on performance fades away with increasing days of sleep loss, but becomes prevalent again during the first few recovery days (Figure 8). In Figure 2, we observed that

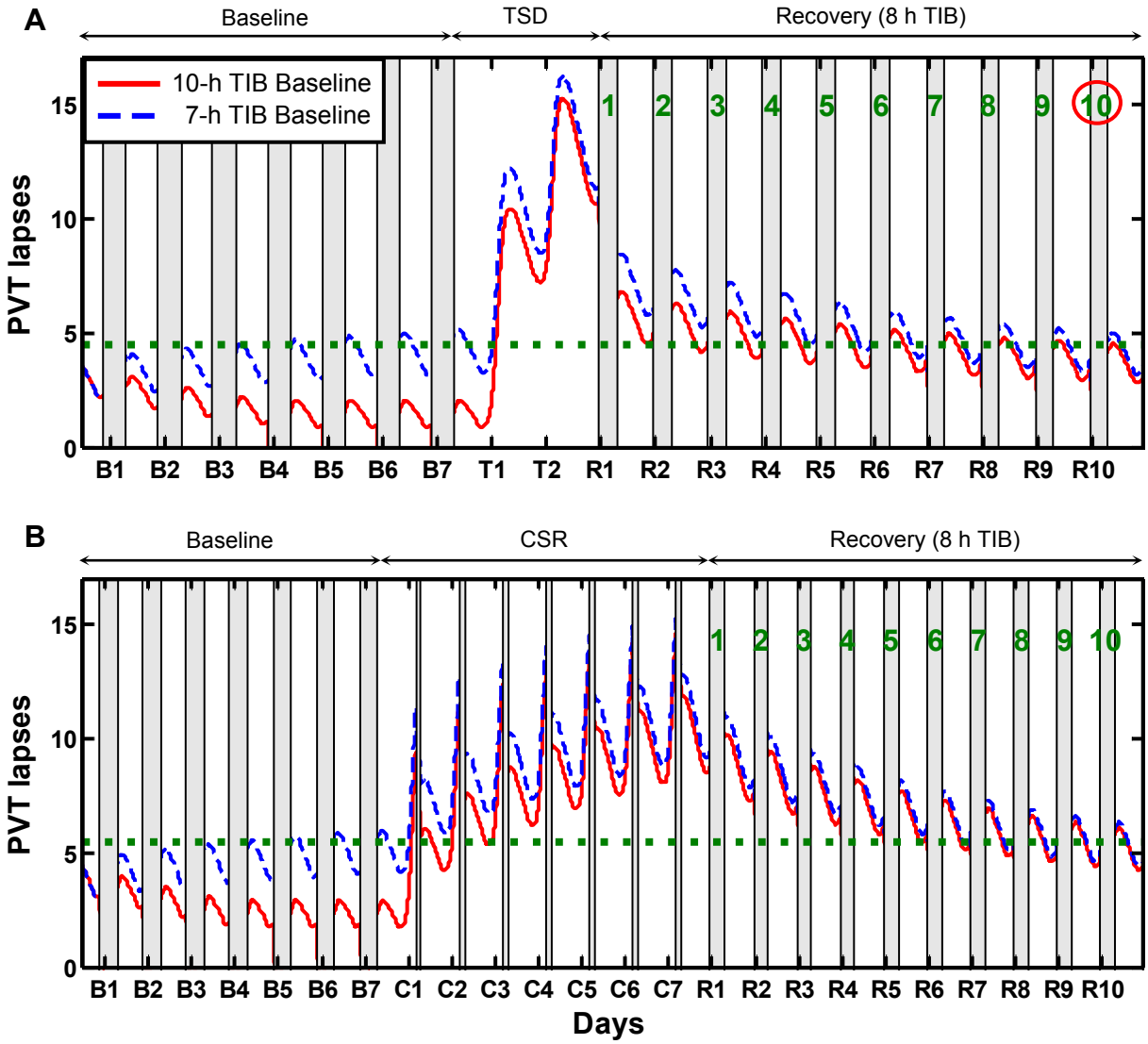

Figure 8—Unified model of performance (UMP) simulations for baseline (B1–B7), chronic sleep restriction (CSR; C1–C7), and recovery (R1–R10) phases under two different baseline conditions for *Study V1*.[8] Panels A and B correspond to the 64-h TSD and 3-h time in bed (TIB) CSR study conditions (5–6; Table 1), respectively. Solid red and dashed blue lines represent UMP predictions for the 10- and 7-h TIB baseline conditions, respectively. The dotted green horizontal line corresponds to the threshold used to define complete recovery (within 20% of the maximum basal performance level). Gray-shaded vertical bars represent the sleep episodes. Also indicated, within the red circle, is the number of recovery nights required for complete recovery under the 10-h TIB baseline condition.

the UMP marginally overpredicted lapses during recovery following TSD and CSR. Thus, the UMP-predicted number of recovery nights in the simulations could have been slightly overestimated. Nevertheless, these simulations demonstrate how the UMP could be used to strategically design different baseline and recovery phases for optimal performance maintenance during sleep loss and faster subsequent recovery. Additional studies validating these model simulation results would help further ascertain the generalizability of the UMP model predictions.

Our final objective was to investigate the effect of a split-sleep schedule versus a consolidated sleep schedule. The UMP predicted that, when considering the best and worst performances during wake time in *Study V5*, a split-sleep schedule of 2-h naps (one every 12 h) during an 88-h time interval would be, on average, better than consolidated sleep schedules of 4 h TIB per day (nocturnal or diurnal) (Figure 9). As expected, the split-sleep schedule yielded predicted performance that was better than consolidated nocturnal sleep during the evening hours and better than consolidated diurnal sleep during the morning hours. This result was confirmed in another simulation where we split the 4-h nocturnal sleep in *Study V4* into two 2-h sleep schedules every 12 h (05:00 to 07:00 and 17:00 to 19:00). Importantly, the simulations suggest that, given a fixed TIB/day, split-sleep schedules offer enhanced flexibility for sleep/work schedules while maintaining performance at similar levels.[22,23] One of the underlying assumptions of these UMP simulations is that the recuperative effect of sleep on performance is independent of the time of day. Although there are reports that suggest otherwise[25,26], to date, experimental data

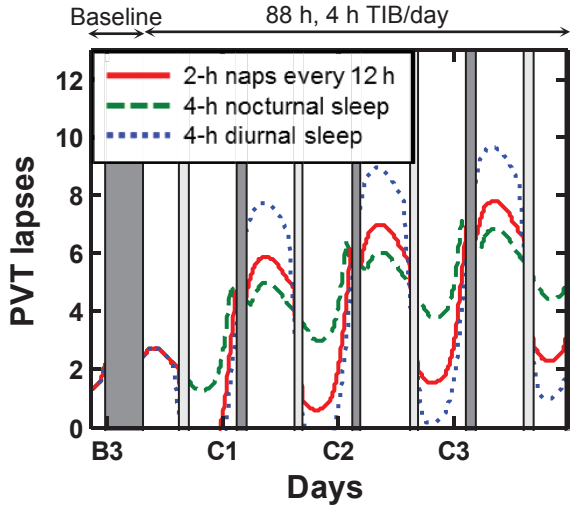

Figure 9—Unified model of performance (UMP) simulations for baseline (B3) and three 4-h time in bed (TIB)/day schedules (C1–C3) across 88 h: (1) solid red line: split sleep with 2-h naps (one every 12 h) as in *Study V5* (study condition 18; Table 1)[14]; (2) dashed green line: consolidated 4 h nocturnal sleep (01:45 to 05:45); and (3) dotted blue line: consolidated 4 h diurnal sleep (13:45 to 17:45). The dark- and light-gray-shaded vertical bars represent the nocturnal and diurnal sleep episodes, respectively, corresponding to the split-sleep schedule.

available to quantify the effect of circadian phase on the recuperative effect of sleep on performance are sparse.

The UMP was derived as an extension to Borbely's[1] seminal two-process model of sleep regulation with the intention to capture the effects of TSD and CSR in one unified framework, wherein the lower asymptote of the homeostatic process was modulated as a function of extant sleep debt. Recently, McCauley and colleagues[27] proposed a state-space modeling approach that represents the two-process model as a system of coupled, nonhomogeneous, first-order ordinary differential equations, where the upper and lower asymptotes of the homeostatic process are modulated based on sleep/wake history while maintaining a fixed difference between them. Although these two models represent extensions of the two-process model, they are structurally distinct and such differences lead to different predictive ability in certain sleep/wake schedules. For example, when we compared the ability of the models to learn group PVT performance under one condition (64 h of TSD in *Study V1*) and then predict the same group's performance under a different condition (CSR of 7 nights of 3-h TIB in *Study V1*), the UMP model was significantly more accurate (> 75%) than the state-space model.[5] In particular, the state-space model predicts that performance continuously degrades under the CSR condition. This is due to the bifurcation characteristic in this model, which stipulates that when daily wakefulness is maintained below a critical threshold (20.2 h), performance converges to a stable level, whereas when daily wakefulness is increased beyond this threshold, performance continuously degrades over time. In contrast, the UMP does not assume the existence of such bifurcation. Rather, it seamlessly bridges the continuum of sleep loss—from CSR to TSD—by modeling TSD as a limiting case of CSR and converging to the two-process model when TIB approaches zero. In this simulation, the UMP was also 20% more accurate than the two-process model.[5]

In other sleep/wake schedules, the structural differences between the two models did not seem to affect their predictive ability; both models yielded comparable predictions, which were better than the ones obtained with the original two-process model. For example, in *Study T1*, the UMP and the state-space models captured the dose dependence of sleep loss and PVT performance reasonably well and significantly better (> 35%) than the two-process model.[5]

More recently, McCauley and colleagues[13] updated their state-space model by incorporating a time-dependence in the circadian amplitude to better account for the effects of night-shift schedules and daytime naps. Although the UMP has not been validated on studies involving night-shift schedules, and it is not clear how it would perform in such schedules, it has been able to accurately predict the effects of daytime naps (*Study V5*). In fact, when compared with the updated state-space model results reported by McCauley and colleagues, it showed a significant improvement (51%). When we compared the UMP predictions against the updated state-space model for two additional sleep/wake schedules used here and by McCauley and colleagues, we noted that the state-space model yielded more accurate predictions (19%) for the TSD schedule in *Study V2* and equivalent predictions for the CSR schedule in *Study V4*.

The UMP was developed using PVT performance data. Consequently, the extent to which its predictions generalize to other aspects of neurobehavioral performance or behavioral tasks is not known. For example, prior studies have found that an individual's relative rank on the PVT was not the same as that individual's relative rank on other neurocognitive tasks.[8,28] However, the PVT is more widely used because it has been shown to be more sensitive to sleep loss than other neurobehavioral metrics.[29] Thus, prior results showing that a person's relative rank on PVT is not correlated with his/her relative rank on other metrics may be due to the lack of metric sensitivity. Accordingly, PVT-based model predictions could only serve as indicators of the likelihood of near-future deficits in other aspects of neurobehavioral performance.

Another model component requiring further work regards the phase of the circadian rhythm function. The UMP currently does not change the circadian phase in response to travel across time zones. Given information about the time zone, the phase could be gradually adjusted in a dynamic fashion, such that the rate of change of phase would depend primarily on the magnitude and direction of the time-zone change, duration since travel, and, to a lesser extent, on the sleep schedule in the newer time zone. However, such model revisions would require sufficient performance data from studies involving transmeridian travel, which are difficult to obtain.

The practical utility of biomathematical models, such as the UMP, lies in the user's ability to simulate the effect of any given sleep/wake schedule on performance, without the need to perform additional experimental studies. Underestimating negative performance effect could negatively affect

safety (in the form of performance-related errors and accidents), whereas overestimating negative performance effect could result in overmanning, unnecessary redundancies, inefficient on/off duty cycles, and other cost-ineffective practices. Although biomathematical model predictions are not perfect, they do provide an objective, quantitative means to assess human performance impairment due to sleep loss. In fact, the use of such models in operational settings are becoming more widespread, e.g., the US Federal Aviation Administration utilized model predictions to revise flight-duty periods for aviation crew members.[30] Friedl and colleagues[31] and Raslear and Coplin[32] provide additional examples of the use of models in operational settings.

In summary, this work validates the UMP's ability to predict cognitive performance impairment due to a wide range of sleep-loss schedules investigated in different sleep laboratories. Accordingly, it could serve as a useful tool to design and optimize laboratory sleep-study protocols as well as a key component of fatigue management systems. To enhance the utility of the UMP, we seek to incorporate additional capabilities. In particular, we are developing strategies to integrate the UMP with the recently developed dose-dependent model of caffeine response[33] so as to predict the detrimental effects of total/chronic sleep loss and the recuperative effects of caffeine using a single model. This supports our long-term goal of incorporating these model components into an integrated computational tool that prescribes countermeasures (e.g., the timing of naps and timing and dosage of caffeine), to optimize an individual's neurobehavioral performance and thereby reduce the risk of sleep loss-related errors and accidents. Although many challenges remain, the integrated UMP would provide another step toward the development of a wearable computer-based system or smartphone app that considers an individual's sleep/wake history, current and recent past performance, and caffeine consumption to predict future levels of performance.[34]

ABBREVIATIONS

CI, confidence interval
CSR, chronic sleep restriction
PI, prediction interval
PVT, psychomotor vigilance task
RMSE, root mean squared error
SRTT, simple reaction-time test
TIB, time in bed
TSD, total sleep deprivation
UMP, unified model of performance
US, United States

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