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ACCOUNTING FOR PARTIAL SLEEP DEPRIVATION AND CUMULATIVE SLEEPINESS IN THE THREE-PROCESS MODEL OF ALERTNESS REGULATION

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Mathematical models designed to predict alertness or performance have been developed primarily as tools for evaluating work and/or sleep-wake schedules that deviate from the traditional daytime orientation. In general, these models cope well with the acute changes resulting from an abnormal sleep but have difficulties handling sleep restriction across longer periods. The reason is that the function representing recovery is too steep—usually exponentially so—and with increasing sleep loss, the steepness increases, resulting in too rapid recovery. The present study focused on refining the Three-Process Model of alertness regulation. We used an experiment with 4 h of sleep/night (nine participants) that included subjective self-ratings of sleepiness every hour. To evaluate the model at the individual subject level, a set of mixed-effect regression analyses were performed using subjective sleepiness as the dependent variable. These mixed models estimate a fixed effect (group mean) and a random effect that accounts for heterogeneity between participants in the overall level of sleepiness (i.e., a random intercept). Using this technique, a point was sought on the exponential recovery function that would explain maximum variance in subjective sleepiness by switching to a linear function. The resulting point explaining the highest amount of variance was 12.2 on the 1–21 unit scale. It was concluded that the accumulation of sleep loss effects on subjective sleepiness may be accounted for by making the recovery function linear below a certain point on the otherwise exponential function. (Author correspondence: torbjorn.akerstedt@ki.se)

Keywords Mathematical modeling, Sleep, Sleepiness, Performance

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INTRODUCTION

Mathematical models designed to predict alertness or performance have been developed primarily as tools for evaluating work and/or sleep-wake schedules that deviate from the traditional daytime orientation. In general, these models cope well with the acute changes resulting from an abnormal sleep. However, many work schedules are associated with shortened sleeps over a number of successive days and result in a cumulative sleep debt. Such a chronic partial sleep loss causes a gradual increase in sleepiness that may or may not level off (Belenky et al., 2003; De Pinho et al., 2006; Dinges et al., 1997; Kandelaars et al., 2006; Oginska & Pokorski, 2006; Van Dongen, 2006; Van Dongen et al., 2003). Unfortunately, this gradual sleep loss does not seem to be handled well by any existing model (Van Dongen, 2004). The basic problem is that the existing models overestimate the recovery function during sleep following high levels of sleep loss.

The original (two-process) model was mainly concerned with sleep regulation, and hence with the need for sleep as indicated by fatigue or sleepiness (Borbély, 1982). It comprised two main components. The first represents the homeostatic effects of the time since awakening and amount of prior sleep; the second is a circadian component that reflects the effect of the biological clock on metabolism and performance. The homeostatic factors are generally considered to show an exponential function such that, for example, there is a steep initial fall in alertness after awakening, with a gradual flattening out toward an asymptote of very low alertness after 24 h of wakefulness. The circadian component is usually represented as a 24 h sinusoid function. For a review of present models, see Mallis et al. (2004).

The first model to focus explicitly on sleepiness was inspired by the two-process model of Borbély et al. and was called the Three-Process Model of Alertness (TPM; Folkard & Åkerstedt, 1987) because it included a third, sleep inertia component. It was subsequently expanded to include sleep prediction (Åkerstedt & Folkard, 1996). It has been successfully validated against EEG parameters and a number of laboratory performance tests (Åkerstedt & Folkard, 1997; Åkerstedt et al., 2004). Several other models have been developed to predict sleepiness or fatigue, and most have also been validated against laboratory performance measures (Belyavin & Spencer, 2004; Hursh et al., 2004; Jewett & Kronauer, 1999; Roach et al., 2004). In a recent development, melatonin and light effects on melatonin has been added (St. Hilaire et al., 2007). It general, the models make similar predictions (Van Dongen, 2004); this reflects on the fact that the underlying components of the models are generally also quite similar.

The present work is focused on the further development of the TPM for alertness prediction; which will be referred to here as the *sleep-wake*

predictor (SWP). The SWP comprises a sinusoidal circadian component with an afternoon peak (Process C) and exponential decrease in alertness over the time awake (Process S). Process S is high on awakening, falls rapidly initially, and gradually approaches a lower asymptote. At sleep onset, process S is reversed and called S′, and recovery occurs in an exponential fashion that initially increases very rapidly but subsequently levels off towards an upper asymptote. Total recovery is usually accomplished in 8 h. The third component is a relatively short-lived wake-up or sleep-inertia component, Process W (not used in the present study). The predicted alertness from the SWP is simply the arithmetic sum of the three functions, C, S, and W. This is illustrated in Figure 1, in which wakefulness has been extended throughout the night such that sleep onset does not occur until 07:45 h. The scale of the model ranges from 1–21 (and was originally based on a visual analogue scale), but in practice "3" corresponds to extreme sleepiness, "14" to high alertness, and "7" to a sleepiness threshold (Folkard & Åkerstedt, 1991)

The failure of the various models, including the SWP, to predict the cumulative fatigue associated with chronic partial sleep loss is attributable (Van Dongen, 2004) to the fact that the recovery function during sleep is too steep when high levels of sleep loss occur. By definition, the function approaches infinity when sleep loss is very large (see Figure 1). Thus, the speed of recovery becomes far too great, making it possible to recover infinite sleep loss during an 8 h sleep. This is clearly a major problem when predicting sleepiness and performance impairment under conditions of sleep loss. In the case of the SWP, it is process S′ that permits the too rapid recovery. Thus, there is a need to modify the exponential character of the curve. This requires a "break" in the exponential recovery function (S′) at some level of prior sleep need. This break would prevent an increase in the speed of recovery beyond what is reasonable. This means changing the exponential rise of S′ to a slower, linear one at some point on the S′ function.

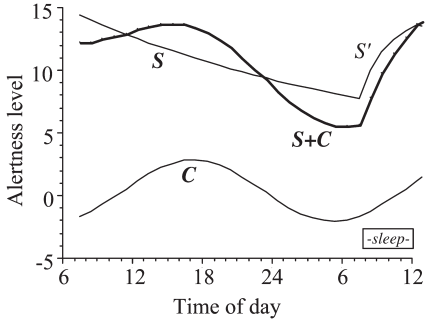

FIGURE 1 The components of the sleep wake predictor/three-process model of alertness regulation.

For the present purposes, we used data from an experimental study in which sleep was restricted to 4 h/day for five successive days. We used the sleepiness self-ratings from this study to determine the position of the break during S′ that would maximize the amount of variance explained by the model.

METHODS

Design and Participants

Data for the modeling were obtained from a recent partial sleep deprivation study. Nine healthy males (age range 23–28 yrs) participated. All were non-smokers, non-obese (BMI range 21–26), and moderate alcohol and coffee consumers, had a normal sleep need (habitual sleep need ranged between 7.0 and 8.5 h), and were not under medication. The study was approved by the local ethical committee at the Karolinska Institute and was conducted in accordance with the Helsinki Committee rules, which conforms with the journal's ethical requirements (Touitou et al., 2006). All participants gave their informed written consent after the procedures had been fully explained. Participants were financially compensated for their participation.

Participants adhered to a sleep schedule with bedtimes at 23:00 h ± 30 min and rise times 07:00 h ± 30 min in their own homes, starting two weeks prior to the first laboratory day. The habituation day (sleep 23:00–07:00 h) was followed by four days in their own homes (sleep 23:00–07:00 h). This was followed by ten days in the sleep laboratory with two baseline days (B1–B2, sleep 23:00–07:00 h), five days with restricted sleep (RS1–RS5, sleep 03:00–07:00 h), and three recovery days (R1–R3, sleep 23:00–07:00 h).

The first rating of sleepiness was carried out after 30 min of remaining in bed after awakening. Thereafter, participants performed a test battery including a 20 min simple driving simulator test, followed by a 6 min reaction-time test. The same procedure was repeated at 14:00 and 20:00 h. Sleepiness was measured by the Karolinska Sleepiness Scale (KSS) directly after each reaction-time test (Åkerstedt & Gillberg, 1990). The question was phrased, How sleepy have you been during the last 5 minutes? Response alternatives ranged from 1 = very alert to 9 = very sleepy, fighting sleep, an effort to remain awake. Level 9 on the scale is physiologically characterized by pronounced intrusions of slow-eye movements and increased alpha and theta-electroencephalographic (EEG) activity (Åkerstedt & Gillberg, 1990). Level 8 has some of these characteristics, while level 7 exhibits the first signs. Below level 7, no sleep-related EEG changes or slow-eye movements are normally seen. The intra-individual correlations between self-ratings and EEG indicators of sleepiness

or reaction time are above r = 0.50 (Åkerstedt & Gillberg, 1990; Gillberg et al., 1994; Reyner & Horne, 1997).

In the laboratory, participants took part two at a time, slept in separate bedrooms, and were allowed to watch videos, play games, read books/magazines, use the Internet, carry out light work, or study. In order to increase ecological validity, participants spent time outdoors at least twice each day (between 09:00 and 19:00 h). Participants abstained from alcohol during the entire protocol and refrained from hard physical activity at least two days before coming to the laboratory. Participants slept (total sleep time, TST) on average: 7.15 ± .07 h on the two baseline days, 3.86 ± .03 h on the five days with sleep restriction, and 7.42 ± .07 h on the first three days of recovery. The light level in the laboratory was around 75 lux, and the outdoor visits involved normal daylight intensity.

Modeling

The basic parameters of the model are (default values within parentheses):

$$S = la + (sw - la) \times e^{(d \times dt)},$$

where la = low asymptote [2.4] m (mesor, see below), sw = S at waking up, d = decay [−0.0353], and dt = Δ time since waking up, in decimal hours.

$$S = ha - (ha - ss) \times e^{(g \times dt)},$$

where ha = high asymptote [14.3], ss = S at falling asleep, and dt = Δ time since falling asleep, in decimal hours. Also,

$$g = \mathrm{Log}((ha - 14.0)/(ha - 7.96))/8$$
$$C = m + a \times \cos((\pi/12) \times (t - p)),$$

where m = mesor [0], a = amplitude [2.5], t = time of day, in decimal hours, and p = acrophase (peak time), in decimal hours.

$$U = m + a \times \cos((\pi/6) \times (t - (p + 3))),$$

where m = mesor [−0.5], a = amplitude [0.5], and t = time of day, in decimal hours, and p = acrophase of C, in decimal hours.

Predictions were derived from the model using a break function at values of S′ varying across the range of values possible with the present amount of sleep loss (i.e., from 6.0 to 14.2) and in steps of 0.1. Predictions were derived using both the complete model and the model with Process W excluded. In the latter case, we also excluded the early morning ratings (before 08:00 h).

In order to estimate the optimal value of S′ at which to apply the break function, regression analyses were performed to evaluate the fit of the predictions in terms of the smallest root mean squared error (RMSE). The analyses were performed on the complete dataset (all sleeps), during sleep deprivation (4 h sleeps), and during normal sleeps (8 h sleeps). Because the original SWP model was developed using group mean data, our initial approach was to apply a set of standard linear regression analyses on group mean data. To evaluate the model at the individual participant level, a set of mixed effect regression analyses was performed. These mixed models estimate a fixed effect (group mean) and a random effect that accounts for heterogeneity between participants in the overall level of sleepiness (i.e., a random intercept; Van Dongen et al., 2004b).

RESULTS

The results indicated that varying the level of process S′ at which the break function was applied had a substantial impact on model fit (see Figure 2). The optimal fits were obtained when the break was applied at a level just above 12 for most estimates. Applying the break at the higher levels of S′ resulted in a strong decrease in model fit. The values of S′ at which the break resulted in the best fit are summarized in Table 1. Inspection of the table indicates that a break level of 12.2 was optimal for both the group mean estimates and the mixed-effect estimates when all sleeps were included in the analysis using the SWP predictions from the model without process W and the ratings prior to 08:00 h. The constant (a) and coefficient (b) for the linear transformation between the alertness score predicted by the model and the KSS ratings were estimated to $a = 8.54$ and $b = -0.37$. Very similar estimates were obtained when all time points were included in the complete SWP model.

The optimal level at which to apply the break function was confirmed for the 8 h sleeps. However, the results were more complicated for the 4 h sleeps, where the group mean estimates suggested a lower break level and mixed-effect estimates suggested a slightly higher level. The two new functions for process S (New S1 and New S2) did not improve the model fit in any of the estimated models.

Figure 3 illustrates the fit of the revised model with the new break function applied to process S′ to the KSS ratings obtained in the study. The revised model closely mirrored both the gradual increase in sleepiness due to partial sleep deprivation and the gradual reduction of sleepiness during the recovery days. It should be noted that the slight phase difference between the predicted and obtained ratings each day probably reflects the schedule of tasks undertaken by the participants.

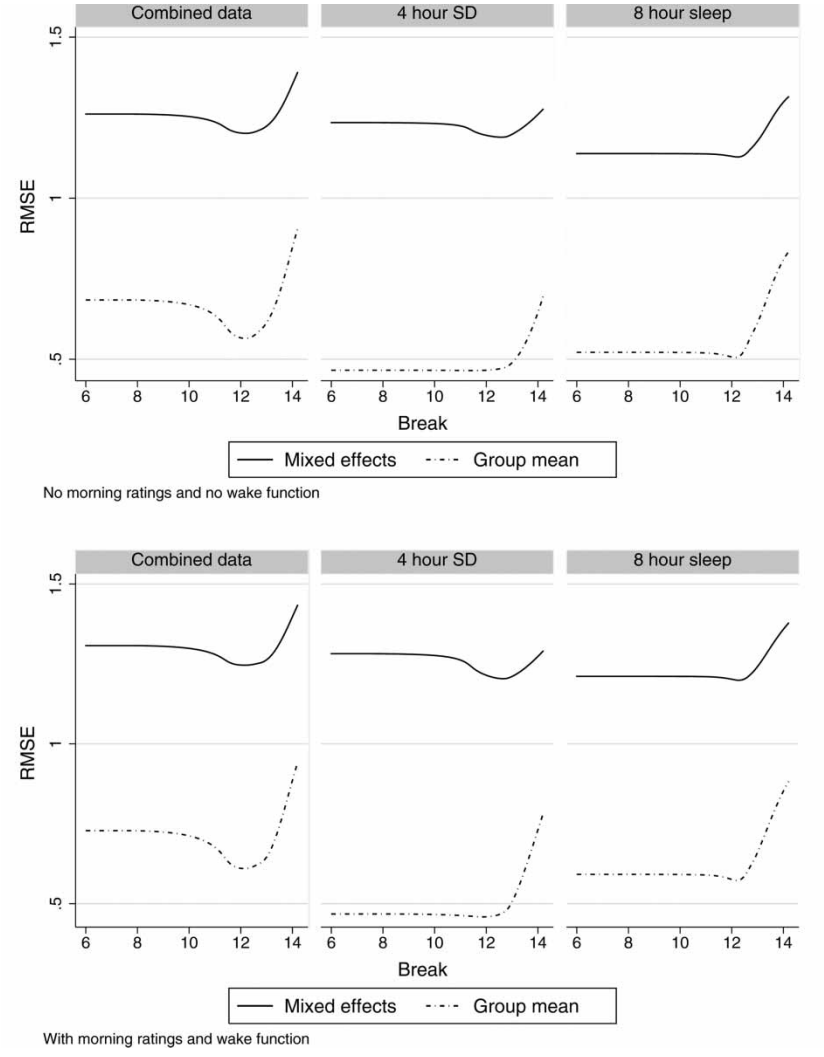

FIGURE 2 Model fit (root mean squared error, RMSE) as a function of level at which the break was applied to S′ for all sleeps, only 4 h sleeps, and only 8 h sleeps, respectively. The left-hand panel shows the model, less process W, applied to the data points after 08:00 h. The right panel shows the complete model applied to all the data points during the day.

DISCUSSION

Our results clearly indicate that introducing a break function to the recovery during sleep can substantially improve the model fit during partial sleep deprivation. The optimal point at which to apply the break function was found to be at an alertness value of 12.2 on the 21-point scale used in the SWP. This value was found to be optimal for the complete dataset comprising both 8 h and 4 h sleeps. The results were rather more

TABLE 1 Summary of Results from Model Selection Test

	Mixed model				Group mean			
Model/data	Br	a	b	RMSE	Br	a	b	RMSE
All sleeps								
Less process W	12.2	8.54	−0.37	1.20	12.2	8.54	−0.37	0.56
Complete model	12.2	8.81	−0.40	1.25	12.1	8.94	−0.41	0.61
4 h sleeps								
Less process W	12.6	8.04	−0.35	1.19	11.5	9.20	−0.45	0.46
Complete model	12.7	8.26	−0.40	1.20	11.9	9.39	−0.49	0.46
8 h sleeps								
Less process W	12.2	9.99	−0.50	1.13	12.2	9.86	−0.49	0.51
Complete model	12.3	9.74	−0.49	1.20	12.2	9.75	−0.49	0.57

Abbreviations: Br = break value, a = intercept, b = regression coefficient, RMSE = root mean square error

complicated when only a subset of the data was used (namely, the days involving either only 4 h or only 8 h sleeps). This finding suggests that the optimum value at which to apply the break function might be slightly different for different sleep lengths. However, there is a complication in interpreting the differences between the estimates in that not only the break function was varied, but the estimated coefficient (b) and intercept (a) also varied across the models. Thus, the best fitting model involves the optimal level of each of these parameters in describing the data.

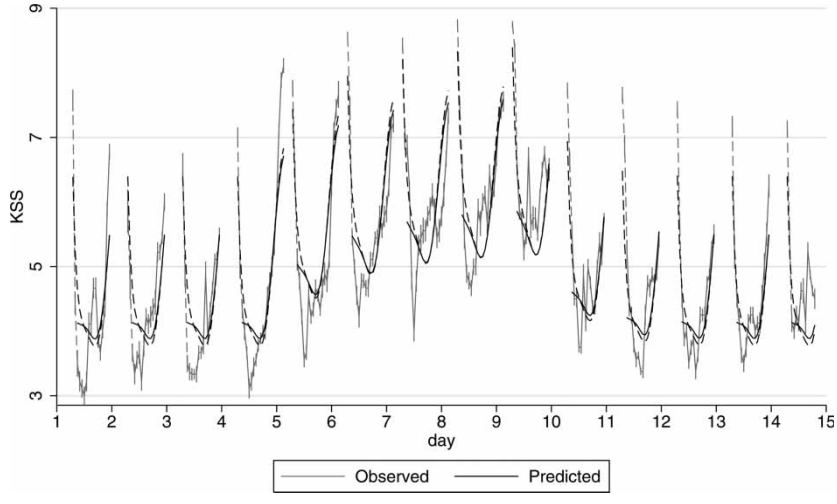

FIGURE 3 Observed and predicted sleepiness on the Karolinska Sleepiness Scale (KSS) based on the final model, less process W (break = 12.2, a = 8.54, b = −0.37). Dashed lines indicate the early morning ratings (07:00–08:00 h) and the predictions derived for the complete model.

Our results indicate that the model predicts both the increase in sleepiness during sleep deprivation and the decrease during recovery with considerable accuracy. This was a major problem with the SWP model before the inclusion of the break function. Thus, although the break function may or may not accurately describe the underlying mechanisms in sleepiness, it does seem to provide a reasonable compromise that should work on data sets that include both full and restricted sleep durations. Future work will have to establish whether the optimal break position should vary depending on the amount of sleep loss. There might, of course, be other non-exponential functions that might describe process S′ more efficiently. This will also have to be determined in future work.

The estimated parameters in the linear transformation between alertness score and KSS ($a = 8.54$, $b = -0.37$) were different from the theoretically assigned values ($a = 10.9$, $b = -0.6$), which is natural because the empirical data describe the mean of manifest sleepiness over all measurement occasions and participants, while the theoretically assigned values correspond to a latent sleepiness level unaffected by contextual factors. The empirical data, though, are the sum of the latent sleepiness across measurements and participants plus the sum of all the contextual factors added to the data. Thus, the coefficient will be smaller to cover a more narrow range of sleepiness.

The present study has several limitations. Firstly, the number of participants is modest and limited to healthy young adults. As suggested by Van Dongen et al. (2003, 2004a, 2004b, 2007), the response to partial sleep loss differs between individuals in a trait-like way. The origins of such differences have not been established, however, and it does not seem possible at present to introduce such model components to improve the prediction of sleepiness or performance on the individual level. For comparison, in a recent study, we validated the model prediction (including the present break function) against individual sleepiness ratings in shift workers and found a relatively good correspondence (mean $r = 0.55$, $p < .01$) using the model default values (Åkerstedt et al., 2007). Still, accounting for individual differences will be an important future task. In any case, the obtained parameters in the present study need to be validated in a new group, and preferably in several groups, obtaining different amounts of sleep/day. One may also discuss the value of predicting subjective sleepiness instead of, for example, performance. The reason for this choice is that the SWP/TPM was developed to predict exactly this variable. Performance measures have been used for validation in previous studies and will be addressed in future work.

In summary, the present study has shown that modifying the exponential recovery function (S′) of the SWP/TPM yields a good fit to the gradual increase in sleepiness across days of restricted sleep and to the subsequent decrease in sleepiness over recovery days.

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