Experimental separation of time of day and homeostatic influences on sleep

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Åkerstedt, Torbjörn, Ken Hume, David Minors, and Jim Waterhouse. Experimental separation of time of day and homeostatic influences on sleep. Am. J. Physiol. 274 (Regulatory Integrative Comp. Physiol. 43): R1162–R1168, 1998.—The purpose of the present study was to evaluate the simultaneous effects on sleep of prior time awake (PRW) and time of day (TOD). Eight male subjects spent 13 days in an isolated sleep lab and had three 8-h baseline sleeps and then 18 4-h sleeps, distributed to provide three sleeps starting at 2400, 0400, 0800, 1200, 1600, and 2000. The three sleeps were preceded by 4, 8, and 12 h of PRW, respectively. ANOVA showed that TST and subjective sleepiness increased with PRW and with closeness to the trough of the circadian rhythm of rectal temperature, whereas sleep latency showed the opposite pattern, and rapid eye movement sleep (REM) latency strongly decreased with PRW and with closeness to the trough. Slow-wave sleep (SWS) increased with PRW, whereas SWS latency and final time awake decreased. REM sleep increased with closeness to the circadian trough, and time awake decreased. Multiple-regression analysis showed that REM latency was closely related to increased SWS in the first sleep cycle, reduced SWS latency, and increased PRW [short PRW before sleep at noon yielded an extremely short (14 min) REM latency]. Sleep latency and final time awake showed almost exactly the same relationship to TOD and PRW. It is concluded that both homeostatic and circadian influences simultaneously affect sleep, that REM latency is very sensitive to the need for SWS, and that the circadian acrophase strongly interferes with sleep. It should be emphasized that the conclusions should not be extrapolated to longer (>12 h) wake spans.

regulation; rapid eye movement sleep; slow-wave sleep; sleepiness; circadian sleep

IRREGULAR SLEEP/WAKE PATTERNS have very strong effects on sleep (2), apparently due to the temporal position of the bedtime. Thus the duration of sleep is usually a function of the time of day, such that sleep displaced from the night decreases in length with increasing displacement from the night hours (4). Similar relationships are seen under conditions of long-term (~1 mo) temporal isolation, if spontaneous desynchronization occurs between the sleep/wake rhythm and the circadian rectal temperature rhythm. Sleep begun at the beginning of the rising phase of the temperature rhythm will be short and sleep begun at the start of the falling slope will be long (12, 27, 33). If desynchronization does not occur and the two variables exhibit the same period, although exceeding 24 h, sleep tends to be started shortly before the minimum and to be terminated shortly before the acrophase (maximum) of the body temperature rhythm (12, 27, 33). Desynchronization of the sleep/wake and temperature rhythms may also be “forced” by scheduling sleep/wake with a period substantially deviating from 24 h, for example 28 or 22 h. The results are essentially the same as for spontaneous desynchronization (16, 17).

Apart from the circadian influence, one would also expect homeostatic factors to affect sleep, but no conclusive data are available. Attempts to use isolation studies (with spontaneous desynchronization) for estimates of homeostatic effects have failed because of confounding by the strong circadian influences. Thus the strong bias of sleep termination to occur toward the circadian acrophase will affect the subsequent duration of wakefulness and the timing of the next bedtime. Also, bedtimes have a strong tendency to occur around the circadian nadir (12, 27) and then to be preceded by a short prior time awake, whereas remaining bedtimes tend to occur around the acrophase and be preceded by a long prior time awake (27). Thus the circadian and homeostatic influences are highly interdependent in an uncontrolled way, making it virtually impossible to separate the effects of the two on sleep.

An alternative approach for studying homeostatic effects is to vary the amount of time awake before sleep experimentally while controlling for the time of day and avoiding the confounding of phase changes. Part of this approach has been implemented in studies with very short (naplike) sleep/wake cycles (11, 28, 31). However, much of the effect on sleep was due to variations in sleep latency because of the shortness of the naps. Another study, providing 0, 2, 4, or 8 h of night sleep, yielded 4.5–1.9 h of sleep after a bedtime at 1100 (with spontaneous sleep termination) (5). However, this study only looked at one time of day, and to our knowledge no study has assessed the relative importance of circadian and homeostatic sleep regulation in an orthogonal design, that is, controlling for circadian influences while studying homeostatic ones and vice versa. In another study of 6-h sleeps distributed across different times of day and with 0–18 h of prior time awake, multiple-regression analysis (MRA) showed that total sleep time (TST) was equally influenced by circadian phase and prior time awake (6). This study did not, however, have an orthogonal design with respect to time of day and prior time awake.

With respect to sleep stages, there is substantial evidence of a strong influence of prior time awake, but little influence of time of day, on slow-wave sleep (SWS;
METHODS

versa. each factor while keeping the other constant and vice versa. The results should yield information on the effects of prior wake and alertness. If appropriately combined, an orthogonal design with three levels (4, 8, and 12 h) of prior time awake on sleep parameters with the use of gate the effects of time of day (in 4-h intervals) and prior wakefulness. However, little is known about the effect of short periods of sleep (stage REM), on the other hand, is clearly dependent on circadian phase, such that more REM occurs at the nadir of the temperature rhythm (1, 14, 16, 22, 32) and there appears to be no evidence of a time awake effect. However, most studies have used long wake spans, and very little is known about the effect of short periods of prior time awake. As with sleep length, no experiment has been carried out with experimental control of both circadian and homeostatic factors. The earlier study of irregular sleep by Åkerstedt et al. (6), however, using a nonorthogonal design and MRA, found that REM sleep was strongly influenced by circadian and homeostatic factors, whereas SWS was related only (but strongly) to the latter (prior time awake).

Circadian and homeostatic effects also affect subjective alertness, which falls gradually during sleep deprivation while being modulated by circadian influences (20). Later studies have found the same phenomenon in connection with forced desynchronization (18). However, little is known about the effect of short periods of prior wakefulness. The purpose of the present experiment was to investigate the effects of time of day (in 4-h intervals) and prior time awake on sleep parameters with the use of an orthogonal design with three levels (4, 8, and 12 h) of prior wake and alertness. If appropriately combined, the results should yield information on the effects of each factor while keeping the other constant and vice versa.

RESULTS

Figure 2 shows the hourly values of the rectal temperature rhythm, represented as a grand average of the six clock times, 2400, 0400, 0800, 1200, 1600, and 2000. Before each of these clock times prior wake time was 4, 8, or 12 h. The order of sleeps was randomized, but all subjects followed the same pattern.

Sleep was always attempted in the dark and was not allowed at other times. A closed-circuit television camera checked adherence to this protocol. It also revealed that during wake times the subjects were sedentary almost the whole time and in normal lighting (300 lx). During the wake time subjects could choose what they did (apart from when they performed psychometric tests, to be reported on later). Their activities were talking, reading, listening to music, and watching television. Meals were chosen and prepared by the subjects, but their composition was similar throughout the experiment and, as far as the protocol would permit, reflected the habitual time and content for breakfast, lunch, and evening meal.

Rectal temperature was measured by a thermistor probe inserted 10 cm beyond the external anal sphincter and recorded automatically (Squirrel Data Loggers, Cambridge Instruments) every 6 min. In the present analysis only hourly recordings have been used. Temperature data had masking effects from activity removed through a previously described method of "purification" (24). Sleep was recorded through Medilog 9000 recorders (Oxford Instruments). The electroencephalogram was obtained from a C3A2 derivation and conventional electrooculogram and electromyogram derivations. The sleep records were scored in 30-s intervals by standard methods (26). The number of awakenings was also expressed as mean length of the sleep segment between awakenings [TST/(awakenings + 1)]. An awakening was defined as stage 0 preceded by at least 5 min of stage 2, 3, 4, or REM sleep.

The effects of time of day and amount of prior sleep (and their interaction) were tested through a two-factor ANOVA for repeated measures (31a), the factors being the prior time awake (4, 8, or 12 h) and the time of day (of midsleep: 0200, 0600, 1000, 1400, 1800, 2200). The results were corrected for sphericity using the epsilon coefficient of Greenhouse-Geisser. To test for a possible accumulative effect across days (for example sleep loss), linear contrasts were applied to all significant ANOVA results. To study intraindividual covariation between variables, simple and MRA were computed on pooled data (all subjects and sleeps) but with dummy variables for n–1 individuals forced into the regression to control for individual differences.

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Two groups of four male subjects were studied in an isolation chamber in which the temperature and humidity were controlled and no traffic noise or other external times cues were present. A clock was present that dictated the subjects’ lifestyle and helped maintain the original phase. The sleep/wake protocol is shown in Fig. 1. Subjects were given the protocol at the start of the experiment so that they could plan their meal times, etc. After control days on a conventional sleep/wake schedule, a sequence of 4-h irregular scheduled sleeps lasting for 9 days was begun. This consisted of 18 4-h sleeps arranged so that, in total, one-third of the time was allocated to sleep. Three sleeps were started at each of the six clock times, 2400, 0400, 0800, 1200, 1600, and 2000. Before each of these clock times prior wake time was 4, 8, or 12 h. The order of sleeps was randomized, but all subjects followed the same pattern.
across individuals (both waking and sleeping) and then averaged across the experiment. The pattern is highly significant ($F = 25.1, P < 0.001, \epsilon = 0.72$) when collapsed into six bins per day and represented at the midpoint of each sleep episode. To check for change in the acrophase of rectal temperature across the experiment, cosinor analysis (25) was applied to the individual 24-h purified curves. A regression line was fitted through the acrophases for each subject, and the mean $\beta$-coefficient was used to compute the $\tau$, yielding a value of $24.15 \pm 0.06$. This corresponds to a time of maximum acrophase of circadian rhythm of $19.2 \pm 0.05$ and $20.4 \pm 0.07$ for days 1 and 9, respectively ($P < 0.05$ for 2-tailed t-test).

Two-factor ANOVA. Table 1 and Figs. 3 and 4 show the results from the two-factor ANOVA. Most main factors showed significant effects, but none of the linear contrasts reached significance and are excluded from the tables. Among the sleep propensity variables (Fig. 3), TST and sleep latency showed a strong significant effect of prior time awake and time of day. TST increased and sleep latency decreased with prior time awake, whereas the longest sleep occurred around 1000 and the shortest latency a little later. Final waking decreased significantly with prior time awake. Stage wake + movement time (WM) showed a moderate effect of both factors, decreasing with prior time awake and reaching a peak around 2000. Mean sleep segment length showed significant effects of both factors plus interaction. Sleep segments increased in length with prior time awake and with closeness to the morning/late night hours. Rated sleepiness increased significantly with increasing time awake and showed a significant time of day pattern, peaking between 8 and 12 in the morning.

Among the sleep stages, SWS (Fig. 4) showed a highly significant increase with prior time awake, as well as a weaker, but still significant, effect of time of day, peaking at 0600. REM, in contrast, showed a highly significant effect of time of day with a peak at 0800 and a weaker, but still significant, effect of prior time awake. The relationship was curvilinear, however, with highest levels for intermediate prior waking. Stage 2 showed a weakly significant effect of time of day, peaking at 0800. Stage 1 showed a significant fall with prior time awake and a significant effect of time of day, with a peak at 0800. None of the interactions was significant.
The latency to SWS decreased significantly with increasing time awake, whereas the latency to REM sleep increased significantly. SWS latency lacked a significant effect of time of day, whereas that of REM latency was significant, with a minimum around 1200.

The amount of REM in the first cycle was weakly affected by the time of day and prior time awake, whereas the amount of SWS in the first cycle increased with increasing time awake and showed effects of time of day, with a minimum at 1400. The duration of cycle 1 was not affected by the two main factors. Cycle 2 could not be analyzed because several sleep episodes were terminated before completion.

The relative amount of SWS showed a highly significant effect (increase) of prior time awake and a moderately significant effect of time of day, with a peak around 2400–0400. Percentage of REM showed moderately significant effects of prior time awake (decrease) and time of day (peak at 0800). Both relative measures (SWS and REM) followed the absolute values and are not shown in Fig. 4.

Across the experiment the mean 24-h TST was 440 ± 8.2 compared with the 464 ± 7.6 min for the last baseline day [P < 0.01, t-test, degree of freedom (df) = 7]. For SWS, the mean was 100 ± 12.3 compared with 62 ± 11.8 min (P < 0.001), and for REM the mean was 85 ± 6.5 compared with 100 ± 5.6 min (P < 0.05). Thus the experiment yielded somewhat less TST and REM but considerably more SWS than baseline.

Relationships between variables. To understand the dynamics of the variation of some key sleep parameters a number of MRA were carried out with pooled data after forcing dummy variables, representing individuals, into the regression. First what aspects of sleep continuity that would account for reduced TST (from the assigned 4 h) were analyzed. Final time awake turned out to be the major contributor, but sleep latency was also significant (Table 2). The third attempted predictor, WM, failed to enter the regression.

To study the relationship between the main sleep parameters we used the MRA technique to compute partial correlations between the parameters, with individuals again forced into the regression as dummy variables (Table 3). TST was highly correlated with REM, stage 2, and SWS. REM and SWS were not significantly correlated, whereas stage 2 was weakly correlated with both. Because of the high correlation of all three variables with TST we also computed correlations for the percentages (of TST) of the sleep stages. Percentages of SWS and REM had a correlation of r = −0.20 (P < 0.05), percentages of SWS and stage 2 r = −0.16 (P < 0.05), and percentages of REM and stage 2 r = −0.09 (NS).

To study the covariation of the delimiting aspects of sleep, sleep latency and final time awake, a partial correlation (as above) was computed between the two. However, because the two variables would normally be almost 4 h apart, it would not be appropriate to select the entries for each pair of the regression from the same sleep. Instead, each measure of final time awake was paired with the sleep latency of the sleep that started at the same point in time as the former ended and that had the same scheduled prior time awake. Thus, for

Table 2. MRA: Predictors of TST

<table>
<thead>
<tr>
<th></th>
<th>r²</th>
<th>β</th>
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<tbody>
<tr>
<td>Final wake</td>
<td>0.61</td>
<td>−0.78</td>
</tr>
<tr>
<td>Sleep latency</td>
<td>0.27</td>
<td>−0.52</td>
</tr>
</tbody>
</table>

F = 117, degrees of freedom 9, 134. MRA, multiple regression analysis.

Table 3. MRA: Partial correlations between TST and sleep stages

<table>
<thead>
<tr>
<th></th>
<th>TST</th>
<th>Stage 2</th>
<th>REM</th>
</tr>
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<tbody>
<tr>
<td>Stage 2</td>
<td>0.61‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM</td>
<td>0.58‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SWS</td>
<td>0.47‡</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05; †P < 0.01; ‡P < 0.001.
example, the final time awake of sleep 3 was paired with the sleep latency of sleep 16, and the final time awake of sleep 6 was paired with the latency of sleep 2, and so on (see Fig. 1). The obtained partial correlation (after forcing a dummy variable for each individual but one into the regression) was \( r = 0.33 \) (\( P < 0.01 \)), whereas that between the two variables from the same sleep was \( r = 0.02 \) (NS). For self-rated sleepiness, the corresponding partial correlation with final wake was \( r = -0.23 \) (\( P < 0.05 \)).

To probe the reasons for the reduction of REM latency with decreased prior time awake, we computed partial correlation coefficients (as above) with some relevant variables. This showed that REM latency correlated 0.56 (\( P < 0.001 \)) with SWS in the first sleep cycle, \(-0.33 \) (\( P < 0.01 \)) with SWS latency, and 0.05 (NS) with sleep latency. Thus a long REM latency was closely associated with (much) SWS in the first sleep cycle, as well as with a short SWS latency.

SWS in the first sleep cycle was also used as a dependent variable in an MRA (as above); with REM latency and SWS latency as predictors, the \( \beta \)-weights became 0.56 and \(-0.28 \), respectively (\( r^2 = 0.36; F = 14.3; df = 9,134 \)). Thus SWS in cycle 1 had a closer relationship with REM latency than with its own latency.

To investigate whether prior sleep (which could not be used as a factor of the ANOVA above) influenced subsequent sleep, we computed MRAs using TST, SWS, and REM of the prior sleep as predictors, as well as time awake and circadian phase (Table 4). Circadian phase was expressed as the linear deviation in hours (0–12 h) from the circadian nadir, regardless of direction. The results showed that prior TST or prior REM did not predict any variable. REM latency was predicted only by prior time awake (decreasing with increasing time awake). REM was predicted by circadian phase (decreasing with increasing deviation from the nadir). SWS was predicted by prior wake (increasing) and prior SWS (decreasing). The standardized regression coefficient corresponds to 4.5 min of SWS per hour awake plus a constant of 16 min of SWS. SWS latency was predicted by prior wake, circadian phase (shorter with deviation from nadir), and prior SWS (increasing with more prior SWS).

**DISCUSSION**

As expected, sleep duration was strongly affected by the time of day/circadian phase, as well as by the duration of the time awake prior to sleep. Previous work has demonstrated the effects of these factors independently or combined, but the present study added the information on simultaneous effects. That is, there was a significant effect of time of day at all levels of prior time awake and there was no interaction between the two factors. Probably, however, the short maximum wake span (12 h) and the restriction of time in bed to 4 h will have curtailed the effects somewhat, and generalizations to full sleep episodes or long wake spans should not be inferred. Prior sleep did not appear to have a significant predictor of sleep length. The reason may be that this variable did not vary enough across sleeps to have a distinct effect. This, in turn, may have been due to the design not permitting adequate expression of that variable. Under other conditions it is likely that this variable may be of equal importance to time awake and time of day (5).

The variation of TST across the time of day was related to the circadian phase of rectal temperature, with more sleep when its midpoint was close to the circadian nadir and less when its midpoint was close to the acrophase. This is almost directly the opposite of what has been reported earlier from studies of spontaneous desynchronization in isolation studies (13, 27, 33). Also, the free-run/desynchronization studies are confounded by the strong tendency for short prior wake spans to end with a bedtime at the temperature nadir and long ones to end at the acrophase (27). This means that sleep begun at the nadir would carry a low need for recovery and thus terminate early on the rising phase, whereas sleep started at the acrophase would carry a greater need for recovery, which would help to maintain sleep until further facilitation by the falling phase of the circadian temperature rhythm.

On the other hand, our results are similar to the results of Dijk and Czeisler (16) who used a forced 28-h sleep/wake pattern. Such a design eliminates much of the confounding of homeostatic and circadian influences, because bedtimes are distributed equally across the circadian cycle and with similar amounts of prior time awake. However, our results have a closer relationship between long sleep and the nadir than those of Dijk and Czeisler (16). Probably, this may be due to the shorter wake span in our study; with increasing wake spans one might predict an extended capacity to maintain sleep despite exposure to the rising temperature phase (5). This is further emphasized by the pattern of subjective alertness, which coincided closely with that of sleep latency and final wake. The results suggest that the circadian pattern of alertness is directly related to sleep initiation and termination. The location of maximum sleep propensity to the nadir has also been

**Table 4. MRA: Sleep antecedents and circadian phase as predictors of SWS, REM, and their latencies**

<table>
<thead>
<tr>
<th></th>
<th>( r^2 )</th>
<th>( \beta )</th>
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<tbody>
<tr>
<td>TST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior time awake</td>
<td>0.12</td>
<td>0.36</td>
</tr>
<tr>
<td>Circadian phase</td>
<td>0.11</td>
<td>-0.33</td>
</tr>
<tr>
<td>REM latency</td>
<td>0.05</td>
<td>0.23</td>
</tr>
<tr>
<td>Prior time awake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM</td>
<td>0.17</td>
<td>0.41</td>
</tr>
<tr>
<td>SWS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior time awake</td>
<td>0.36</td>
<td>0.59</td>
</tr>
<tr>
<td>Prior SWS</td>
<td>0.04</td>
<td>-0.18</td>
</tr>
<tr>
<td>SWS latency</td>
<td>0.21</td>
<td>-0.46</td>
</tr>
<tr>
<td>Prior time awake</td>
<td>0.04</td>
<td>-0.22</td>
</tr>
<tr>
<td>Circadian phase</td>
<td>0.03</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Attempted predictors were prior TST, prior REM, prior SWS, prior time awake, and absolute deviation from the acrophase (in hours). Only significant values are entered. Nonsignificant items are left out in three last MRAs. Circadian phase expressed as deviation from circadian nadir.
observed in the studies with short (naplike) sleep cycles, which mainly reflect the influences of sleep latency (11, 28, 31).

The variation of TST across conditions was due mainly to early final awakenings, rather than sleep latency or time awake after sleep onset. The circadian influence on sleep termination is well established (12, 16, 33), whereas the homeostatic influence has not been addressed. The present results clearly indicate that the homeostatic influence will strongly modify (additively) the circadian influence on sleep termination and vice versa.

The second factor accounting for the variation of TST was sleep latency, the homeostatic and circadian influences of which are relatively well established (7). However, the present results demonstrate their simultaneous influence at low levels of prior wake. Thus sleep latency was extremely long (55 min) when evening bedtimes were combined with short periods of prior wakefulness. This level is >2.5 times the maximum value (20 min) of the standard sleep latency test, indicating the insensitivity of this test at the low end of the sleepiness continuum.

Interestingly, there was a correspondance between the circadian regulation of initiation and termination of sleep. Thus long latencies occurred in the same circadian phase as long final wake times (and low subjective sleepiness), but not in the same sleep. Also, both variables decreased with sleep loss. Thus sleep initiation and termination seem to be similarly affected by circadian and homeostatic regulation of arousal; a short prior time awake and closeness to the circadian acrophase will cause either a long sleep latency or an early awakening, depending on whether sleep is scheduled to start or end at this time.

With respect to sleep stages, SWS showed the expected relationships, strong for prior time awake and very weak for time of day (22, 29). The "exchange rate" of minutes of SWS per hour awake (4.5 min SWS/h awake) was in line with that found in previous studies (6, 22, 29). Stage 2 showed a significant but weak effect only for time of day, probably adjusting to the predominant need for SWS (and REM sleep) (30). Also REM sleep showed (in absolute and relative terms) the expected result, a strong effect of time of day (1, 14, 16, 22, 32) but no effect of prior time awake (1, 8, 22).

With respect to latencies to sleep stages, SWS showed the expected reduction with increasing time awake and a virtual absence of circadian effects (22, 29). REM latency showed the expected circadian effect with low values in the morning/noon (1, 14, 22, 32). However, there was also a strong decrease of REM latency with decreasing prior time awake. Together with the circadian effect at the nadir, a short time awake brought the mean REM latency down to 14 min (the maximum was 86 min). This is much shorter than what has been found earlier and similar to what is seen in patients with depression (21). The observed negative relationship of REM latency to sleep loss has no clear precedent, but is supported by findings in several nap studies. Thus, Karacan et al. (23) found that REM latency was reduced to 64 from 117 min in a morning nap (i.e., close to recent sleep) compared with an afternoon nap. A similar observation (a fall from 90 to 57 min) was made by Feinberg et al. (19), who also suggested that REM sleep responds to reduced levels of need for non-REM (NREM) sleep. Furthermore, in a reanalysis of two studies, Campbell and Gillin (10) found that closely preceding sleep seemed to reduce REM latency and increase the duration of the first REM period. The data were interpreted as supporting the hypothesis of the "process S deficiency in depression" (9), that is, the notion that the short REM latency and reduced SWS in depression would be due to too little pressure for NREM or SWS. The preeminent need for SWS being the determinant of REM latency is also supported by the observation in the present study that REM latency was positively correlated with the amount of SWS in the first cycle, but negatively to SWS latency, SWS, thus, seems to expand at the cost of REM onset. Thus it appears that REM onset is homeostatically regulated, but in a negative way, being secondary to the need for, and expression of, SWS. That is, the pressure for SWS appears to take precedence over that for REM sleep.

The circadian pattern of sleepiness is well established, as is the increase in sleepiness with the amount of time spent awake and their combined effects in total sleep deprivation studies (20). However, the present study demonstrated the combined effect of the two in an orthogonal design. Sleep latency varied in an opposite way to sleepiness. Similar results for subjective alertness have been obtained with forced desynchronization (18). It should be emphasized that no interaction was observed between time of day and prior time awake; that is, the increase of sleepiness with time awake was similar regardless of the time of day. Indeed, this was the case for all sleep variables. Thus homeostatic and circadian influences seem to act only additively, at least with the present design.

The amounts of TST and REM obtained per day across the experiment seem to have been only slightly less than what had been obtained in the last control sleep (8 h). In contrast, SWS increased by 50%. This may be due to the fact that the response of SWS to prior time awake describes an exponentially saturating function (8) and that the present study operated at the low end of this relationship, where the relationship may be steeper than in the region of (normal) 16-h wake spans.

It should be emphasized that the present results were obtained with a less-than-perfect design (sleep times were dictated) to study simultaneously homeostatic and circadian influences. On the other hand, the perfect design (with ad libitum sleep) is not feasible practically. Thus, it is necessary to combine the results from the present approach with those of other designs (using spontaneous or forced desynchronization) to obtain an overall impression of homeostatic and circadian influences on human sleep.

In summary, the present study has demonstrated the strong, often simultaneous, influence of time awake and time of day on sleep, without any interactions between the two. The dependence of REM latency on
prior time awake and the covariation of sleep initiation and sleep termination is particularly noteworthy.

**Perspectives**

The demonstration of an independent homeostatic and circadian sleep regulation means that the effects of irregular work/sleep behavior caused by work or leisure activities will result in very variable sleep amounts and recuperation. Thus irregular sleep schedules will often result in the amount of sleep obtained being far less than the time “allocated,” with serious implications for safety and health. The effects seem predictable (3) and the present work on sleep/wake prediction becomes of importance in industry and transport. Another interesting observation is REM onset being strongly and negatively related to the need for SWS, which may have implications for the interpretation of short REM latencies as markers for depression or environmental pressures. Finally, insofar as sleep latency reflects alertness, the extremely long latencies (55 min) at the acrophase after short prior wake spans suggest that alertness can be increased to very high levels compared with normal daytime levels (10–15 min latencies). It is not clear, however, if this has any practical implications in terms of, for example, increased performance capacity. One might expect that very tedious, yet attention-demanding tasks would benefit from strategic sleeping. This issue is easily amenable to experimentation.

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