TIME COURSE OF SLEEP INERTIA AFTER NIGHTTIME AND DAYTIME SLEEP EPISODES

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INTRODUCTION

The transitions between the sleeping and waking state has been the object of interest in physiology. Moruzzi (23; p. 136) concluded that "[a] critical but moderate level of reticular deactivation must be slowly attained in order to permit the onset of the instinctive behavior of sleep. If the fall of the reticular tone occurs abruptly, and/or is too strong, the behavioral result will not be physiological sleep, but coma". The onset of sleep has received much more attention than the emergence from sleep. The present study addresses the latter aspect.

The two factors exerting a major influence on the level of vigilance and performance are the duration of prior waking and sleep, and the phase of the circadian rhythm (20). The constant level of daytime vigilance and performance during the major part of the waking episode has been attributed to the compensation of the declining homeostatic (e.g. sleep/wake dependent) trend by the rising circadian trend (2, 8, 15, 18).

If the duration of waking is extended (e.g. during emergency operations), or if waking and sleep episodes are shifted to a different circadian phase (e.g. during shift work), vigilance and performance may deteriorate. In such circumstances napping can be an effective countermeasure (see 31). However, the immediate benefit of a nap or a regular sleep episode may be reduced by sleep inertia. This term (22) denotes the reduced vigilance and impaired performance during the period that follows upon awakening. It was already evident in early studies that complete behavioral and functional wakefulness may lag behind the sleep/wake transition as reflected by the EEG (21, 34). Sleep inertia and the effects of napping have been mainly investigated in the context of sustained operations involving sleep deprivation and shift work (10, 12, 26, 30). The duration of sleep inertia differed widely ranging from 1 minute (34) to more than 3 hours (16). Although only few attempts were made to quantify its time course (18), sleep inertia has been incorporated in several models of sleep and vigilance (1, 2, 3, 16, 17, 18). A principal aim of the present study was to document its time course in more detail using a protocol that included both nighttime sleep episodes and a daytime nap.

METHODS

Design and data collection.

Nine healthy, male subjects (age: mean 23.8 yr, range 20-26 yr) were recruited from the student population of Zürich and paid for their partecipation. They were all non-smokers and their medical history, current health status and subjective sleep quality were checked on the basis of questionnaires. The adaptation night was used to exclude sleep apnea and nocturnal myoclonus. Subjects consented to refrain from napping, alcohol consumption and drug intake, and to adhere to a regular sleep-wake pattern during the week preceding the experiment as well as during the experiment. The latter requirement was confirmed by wrist activity recordings.

The schedule consisted of two baseline days, a day with a nap in the early evening starting at 18.00 h, and a day after the post-nap night (Fig. 1). The nap was terminated at the onset of the first REM sleep episode or after two hours of sleep. During the day the subjects assessed their alertness and psychomotor performance every two hours on a palmtop computer (PSION OR-GANISER II; 33). During the first hour after awakening from night-time sleep or from a nap, assessments were made every 20 minutes. Subjects were given the opportunity to familiarize themselves with the tests prior to the experiment. Alarms were programmed to remind subjects of performing the tests. After the experiment the recorded data were transferred to a personal computer.

Sleep was recorded polysomnographically during an adaptation night, a baseline night, a nap, and a post-nap night. The sleep EEG was subjected to a spectral analysis and sleep stages were scored according to conventional criteria (29). Sleep related data are reported elsewhere (35).

Alertness and performance.

Alertness was self-rated on a pseudo analog scale which consisted of a 20-point subjective rating scale on a palmtop computer (33). Alertness, date and time of rating were recorded. Performance was measured by a memory search task based on Sternberg's paradigm (32, 33). The subjects were required to memorize a set of 7 letters that appeared simultaneously on the display. They pressed a key to indicate that the set had been memorized. Forty single probe letters then appeared successively on the screen. The subjects were instructed to press the T (true) key if the letter was in the set and the F (false) key if it was not. Each probe letter had an equal chance of being or not being in the set. The following data were recorded: date and time of completion; time taken to memorize the set; number of true positives, number of true negatives, number of false positives, number of false negatives and the corresponding mean reaction times; number of probes not responded to within 5 s. Only the mean reaction time of correct responses (i.e. true positives and true negatives) was used in the further analysis.

Data analysis and statistics.

The SAS statistical package (SAS Instrument Inc, Cary, NC, USA) was used for all statistics.

The analysis of variance (ANOVA) contained the factors 'time interval' and 'condition'. The factor 'condition' consisted either of 3 baseline days (Tuesday, Wednesday, Thursday until the nap; see Fig. 1) and the day after the post-nap night (Friday) when the time course over the entire day was analyzed, or of 3 baseline days, the post-nap hours, and the day after the post-nap night when only the inertia was tested.

In Figures 2 and 3, baseline mean alertness ratings are based on data of Tuesday, Wednesday, and Thursday until the nap; the baseline reaction times do not include the data of Tuesday to minimize the bias due to the practice effect (see Results).

Exponential functions were fitted to the data of the first 3 hours after awakening to estimate the time constant and the extent of the sleep inertia component. The procedure NLIN (nonlinear regression, SAS) was applied, which calculates least-squares estimates of the parameters of a nonlinear model, and asymptotically valid standard errors of the estimates.

As a further measure of the inertia, the difference between the first assessment after awakening and the assessment approximately 3 hours later (at 10.00 h after nocturnal sleep and at 22.00 h after the nap) was determined.
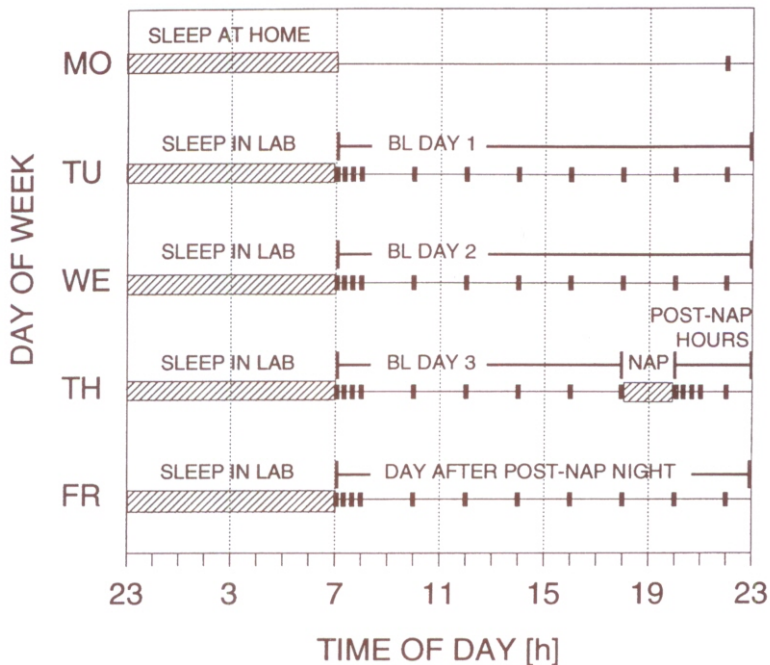
Fig. 1. - *Study protocol.*

Sleep episodes and the nap are indicated by hatched bars, the assessments of alertness and reaction time by vertical lines.

RESULTS

Figure 2 illustrates the time course of alertness and reaction time as a function of time of day. The nap at 18.00 h showed of a total sleep time of 74.9 (8.3, SEM) minutes, and contained 27.6 (5.2) minutes of slow wave sleep; time in bed was 106.7 (10.9) minutes. Both alertness and reaction time showed a flat distribution over the day and a distinct sleep inertia effect. Alertness increased within the first hour after awakening, whereas reaction time declined. In Figure 3 the time course of sleep inertia over the first 3 hours after awakening is depicted. The fitted exponential function is also indicated. The inertia effect subsided after approximately one hour.

1. *Alertness.* - The sleep inertia was evident from the significant contribution of the factor 'time interval' in the ANOVA (analyzing baseline days and the day after the post-nap night; factors: 'time interval', $F_{10,332}=19.15$, $p<0.0001$; 'condition', $F_{4,332}=0.42$, $p>0.5$; interaction, $F_{29,332}=0.82$, $p>0.5$). When the first 4 assessments after awakening were excluded, the factor 'time interval' was no longer significant ($F_{6,204}=1.93$, $p>0.05$).

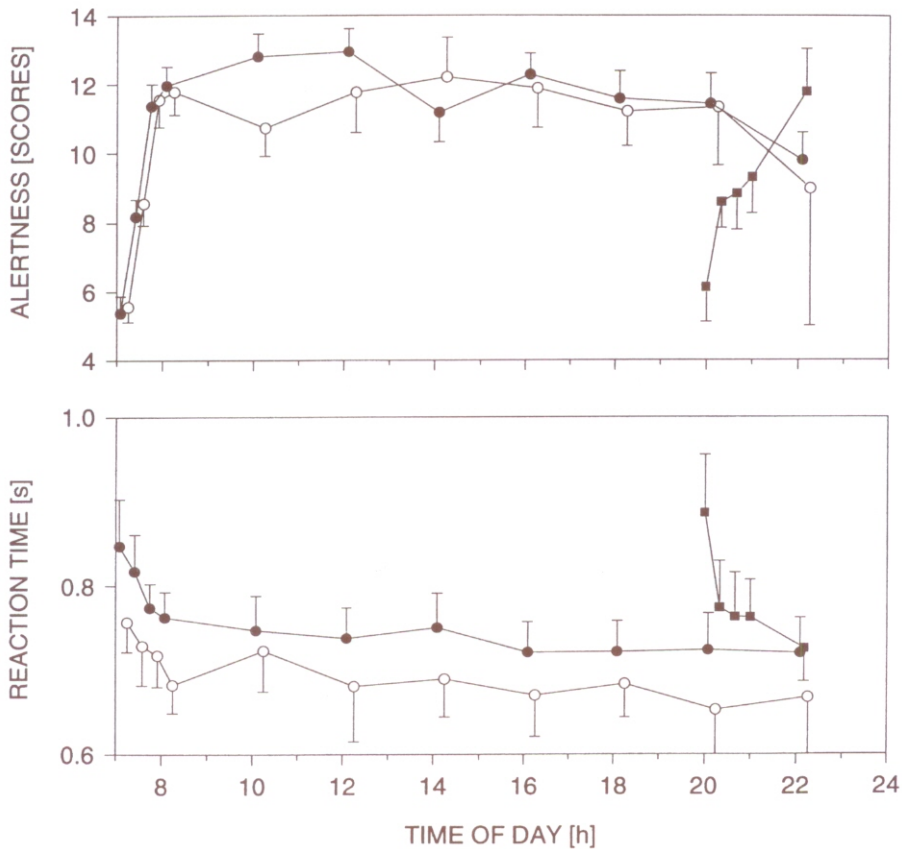Sleep inertia was investigated in detail by considering only the values within the

Fig. 2. - *Time course of alertness and reaction time in a memory task (correct responses).*

Filled circles denote baseline days, open circles the day after post-nap night, and filled squares the post nap hours. Mean values and 1 SEM are plotted. The post-nap data are plotted at the midpoint of 20-minute bins, the other data are shifted by -5 and 5 minutes, to enhance the clarity of the representation.

three hours after awakening. Analyzing the first 4 assessments (baseline days post-nap hours, day after post-nap night) confirmed the sleep inertia by the significant contribution of the factor 'time interval' ($F_{3,153}$=57.34, p<0.0001; 'condition', $F_{4,153}$=1.81, p>0.1; interaction, $F_{12,153}$=1.45, p>0.1).

The time course of sleep inertia was studied by fitting a saturating exponential function to the data of the first 3 hours after awakening. The fit was calculated for each condition (baseline days, post-nap hours, day after post-nap night) separately (range of r^2: 0.25 to 0.69), as well as for the pooled data (r^2: 0.49), and for the pooled mean values of each condition (r^2: 0.80). The latter result is summarized in Table 1, and the resulting function is plotted in Figure 3 (top). The time constants and inertia effects did not differ among conditions (overlapping 95%-confidence intervals).
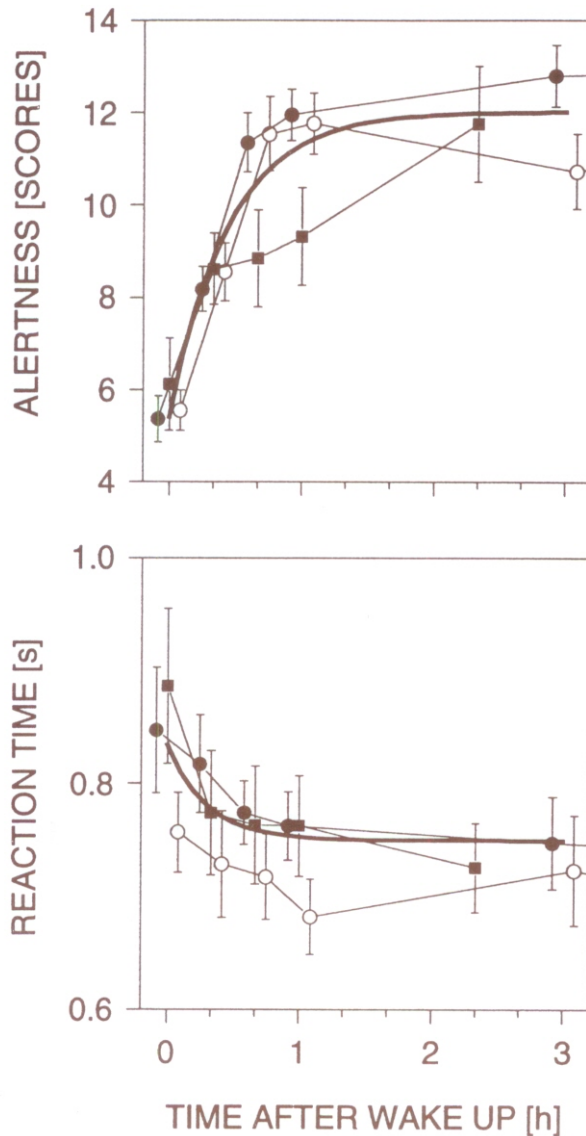
Fig. 3. - *Sleep inertia.*

Time course of alertness and reaction time in a memory task (correct responses) in the first 3 hours after awakening. Mean values ±1 SEM are plotted. The estimated exponential function of the inertia component is indicated by the continuous curve (for parameters see Table 1). Filled circles denote baseline days, open circles the day after the post-nap night, and filled squares the post nap hours. For clarity, the post nap data are plotted at the correct time, and the baseline and post-nap data are shifted by -5 and +5 minutes, respectively.

A further measure of the sleep inertia was obtained by calculating the difference between the assessment 3 hours after awakening and the assessment immediately after awakening. Two values (from 2 subjects) out of 44 non-missing values were

Table 1. - *Quantification of the sleep inertia effects.*

Measure	Alertness	Performance
Time constant [h]	$t_a = 0.45$ (0.11)	$t_{rt} = 0.30$ (0.28)
Asymptotic level [scores or s]	$a_{as} = 12.04$ (0.46)	$rt_{as} = 0.75$ (0.018)
Inertia effect (estimated) [scores or s]	$a_{si} = 6.62$ (0.68)	$rt_{si} = 0.084$ (0.030)
Inertia effect (measured) [scores or s]	7.15 (0.95)	0.095 (0.022)

A saturating exponential function was fitted to the alertness ratings and an exponential function to the reaction time measures in a memory task (correct responses). The estimation procedure was applied to the assessments of the first 3 h after awakening (see text for details). The inertia effect was measured by calculating the difference between the first assessment after awakening and the assessment 3 hours later. Estimated parameter values with approximated SEM (see Methods) or mean values with SEM in parenthesis are indicated.
Equations.
Alertness: $a = a_{as} - a_{si} * exp(-t/t_a)$; a_{as}: asymptotic level; $(a_{as} - a_{si})$: level at awakening; a_{si}: decrement due to sleep inertia; t_a: time constant
Reaction time: $rt = rt_{as} + rt_{si} * exp(-t/t_{rt})$; rt_{as}: asymptotic level; $(rt_{si} + rt_{as})$: level at awakening; rt_{si}: increase due to sleep inertia; t_{rt}: time constant

zero, all others were positive. The resulting mean value is shown in Table 1. The inertia effect did not differ among the conditions (baseline days, post-nap hours, day after post-nap night; $F_{4,39} = 0.8$, $p > 0.5$). The inertia effect after night sleep episodes (mean scores, 7.06 (0.96)) did not differ from the nap sleep value (7.25 (1.75)) (ANOVA, $F_{1,15} = 0.01$, $p > 0.5$).

The level of alertness at 22.00 h was not significantly increased by the nap (ANOVA, factor 'condition' (baseline days, post-nap hours, day after post-nap night), $F_{4,32} = 0.89$, $p > 0.1$). Comparing the mean baseline level (9.11 (0.92) scores) with the post-nap level (11.78 (1.26) scores) also revealed no significant difference (ANOVA, $F_{1,16} = 2.93$, $p > 0.1$).

No significant correlations between the inertia effect and sleep variables (amount of slow wave sleep, mean slow-wave activity, sleep stage preceding awakening) were present. All conditions were analyzed separately.

2. *Performance: reaction time of correct responses.* - On average, the subjects needed 15.9 s (3.38, SEM) to memorize the set, committed 2.5 (0.42) errors (false positive and false negative responses) with a reaction time of 0.49 s (0.054); the reaction time of correct responses was 0.77 s (0.035).

Sleep inertia was evident from the significant contribution of the factor 'time interval' in the ANOVA (analyzing baseline days and the day after a post-nap night; factors: 'time interval', $F_{10,332} = 2.52$, $p < 0.01$; 'condition', $F_{4,332} = 8.07$, $p < 0.0001$; interaction, $F_{29,332} = 0.18$, $p > 0.5$). After excluding the first 4 assessments after awak-

ening, the factor 'time interval' was no longer significant ($F_{6,204}=0.72$, $p>0.5$; 'condition' $F_{4,204}=4.53$, $p<0.05$; interaction $F_{17,204}=0.23$, $p>0.5$).

The significance of the factor 'condition' was due to a practice effect. Mean reaction times per condition (Tuesday 0.82 s, Wednesday 0.77 s, Thursday 0.75 s, Friday 0.70 s) were subjected to Duncans multiple range test. Duncan groupings with no significant difference within groups were Tuesday to Thursday and Wednesday to Friday.

Sleep inertia was studied in detail by analyzing only the values within the three hours after awakening. The analysis of the first 4 assessments (baseline days, post-nap hours, day after post-nap night) showed a significant 'time interval' effect ('time interval', $F_{3,149}=3.11$, $p<0.05$; 'condition', $F_{4,149}=4.38$, $p>0.1$; interaction, $F_{12,149}=0.14$ $p>0.5$).

The time course of sleep inertia was investigated by fitting an exponential function to the data of the first 3 hours after awakening. The fit was calculated for each condition (baseline days, post-nap hours, day after post-nap night) separately, as well as for the pooled data, and for the pooled mean values of each condition. The latter result is summarized in Table 1, and the resulting function is plotted in Figure 3 (bottom). The r^2-values were low ($r^2<0.3$) and the 95% confidence interval of the time constants included zero. The time constants and inertia effects did not differ among conditions (overlapping 95%-confidence intervals).

The inertia effect was also measured by calculating the difference between the first assessment after awakening and the assessment 3 hours later. Out of 45 non-missing values 10 were negative (5 subjects; 7 during baseline days, and 3 after the post-nap night), all others were positive, indicating a greater variability of this measure compared to alertness. The resulting mean value is shown in Table 1. The inertia effect did not differ among the conditions (baseline days, post-nap hours, day after post-nap night; $F_{4,40}=0.52$, $p>0.5$). The inertia effects after night sleep episodes (0.08 s (0.027)) and after the nap (0.13 s (0.039)) did not differ (ANOVA, $F_{1,16}=0.99$, $p>0.1$).

Reaction time at 22.00 h was not significantly shortened by the nap (baseline days, post-nap hours, day after post-nap night; $F_{4,32}=1.38$, $p>0.1$). Comparing the level of Wednesday (0.72 s (0.042)) with the post-nap level (0.73 s (0.039)) revealed no difference (ANOVA, $F_{1,16}=0.01$, $p>0.5$).

Correlations between the inertia effect and sleep variables (amount of slow wave sleep, mean slow-wave activity, sleep stage preceding awakening) were calculated for each condition separately. Significant negative correlations between the inertia effect on one hand and slow wave sleep ($r=-0.79$, $p<0.05$, Spearman rank correlation) and slow-wave activity ($r=-0.73$, $p<0.05$) on the other hand were present for the nap.

No correlation between the inertia effect (defined as the difference between the first assessment after awakening and the assessment 3 hours later) of alertness and reaction time was observed.

DISCUSSION

Both, subjective alertness ratings and performance showed a significant sleep inertia component. In accordance with previous reports (see (11) for an overview of performance studies upon awakening) the data demonstrate that sleep inertia is a robust and reproducible phenomenon.

In accordance with the report of Folkard and Åkerstedt (18), sleep inertia was found in the present study to subside according to an exponential function. If the duration of the effect is assumed to correspond to three time constants, the impairments of alertness and performance persisted for 1.4 h and 0.9 h, respectively. Sleep inertia of alertness was therefore of a somewhat shorter duration than the 2.0 h in the Folkard and Åkerstedt study (18; time constant 0.66 h). In general, sleep inertia was reported to be short lasting (1-15 min, (25); 1-20 min, (11); 5-35 min (5)). Its duration may depend on the variable measured. Some authors have made only one assessment after awakening and the next ones two or more hours later (6, 27), a procedure that does not allow a precise determination of the time course and duration of sleep inertia.

In the present protocol, sleep inertia was determined after a regular nighttime sleep episode, after a nighttime sleep episode with reduced sleep pressure (post-nap night), and a shorter daytime sleep episode. The influence of sleep/wake dependent and circadian factors on sleep inertia is unclear from the literature. On the one hand, sleep inertia was shown to be a function of the duration of prior wakefulness as well as of the circadian phase (13, descending subtraction task; 24, various tasks), while on the other hand sleep inertia for a logical reasoning task (27) was reported to be independent of these two factors. The present results did not reveal any significant differences between the sleep conditions.

Sleep inertia measures of alertness varied less than those of performance and there was no significant correlation between the two. The latter measure is possibly more susceptible to disturbances. Discrepancies between subjective and objective measures are common in the literature (e.g., 14, 19, 28).

Alertness and reaction time were at a constant level throughout the day and there was no significant midday decline. These findings are in accordance with the time course of self-rated sleepiness during the habitual waking episode (28) and with the alertness ratings and cognitive performance during the daytime hours of a constant routine protocol (9).

Napping is an effective countermeasure to the impairment of vigilance and performance (see 10). In the post-nap hours of the present study, no significant improvement of these variables was observed. This may be due to the fact that no extended waking episode preceded the nap. Also, the effect depends on the variable measured. Thus in a study on the temporal placement of naps (14), benefits in reaction time performance but not in self assessed sleepiness were reported.

One of the problems of applying repeatedly performance tests is the practice effect. In the present study, it was manifested by the decrease of mean reaction time over consecutive experimental days. The practice effect may persist even

throughout a long-term experiment (26 days) as has been shown by Totterdell and Folkard (33) for a four-choice serial reaction time task. Nevertheless, in the present study, the progressive increase in performance did not prevent us from delineating the characteristics of sleep inertia.

The data obtained in the present experiments are useful for incorporating the sleep inertia effect in models of sleep and vigilance (for an overview see 2, 7). The results confirm that it is legitimate to approximate the effect by an exponential function as had been originally proposed by Åkerstedt and Folkard (3) in their 3-process model. Various experimental protocols including shift work schedules (3, 4, 18), a forced desynchrony protocol, and a shortened photoperiod schedule (2) were successfully simulated. Two of the present authors advanced a composite model of sleep regulation in which a sleep inertia component was also included (1).

The approach based on the additive interaction of the homeostatic, circadian and sleep inertia processes has proved useful as a first approximation. However, nonlinear (e.g. multiplicative) interactions may also be present. Thus, in a forced desynchrony protocol the contribution of the homeostatic component of alertness and performance was dependent on circadian phase, and the contribution of the circadian component was a function of prior wakefulness (9).

In conclusion, the results of this study clearly show that the rapid reversibility of the sleep state pertains only to a part of the waking functions. Subjective alertness and reaction time in the memory task were considerably impaired after awakening and reached only gradually the typical waking level. It takes time to become fully awake. Thus the progressive transition from waking to sleep which has been so cogently described by Moruzzi (23), has a counterpart in the gradual emergence from sleep.

SUMMARY

Sleep inertia refers to the period of reduced vigilance following upon awakening from sleep. To investigate the time course of sleep inertia, self-ratings of alertness and reaction time in a memory task were repeatedly assessed after nighttime and daytime sleep episodes in healthy young men. Alertness gradually increased and reaction time gradually decreased within the first hour after awakening. Their time course could be described by exponential functions with time constants of 0.45 h and 0.3 h, respectively. The data demonstrate that sleep inertia is a robust, quantifiable process that can be incorporated in models of sleep and vigilance.

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