Performance on the psychomotor vigilance task (PVT) sensitively reflects a circadian modulation of neurobehavioral functions, as well as the effect of sleep pressure developing with duration of time awake, without being confounded by a learning curve. Sixteen healthy volunteers underwent two 40-h constant posture protocols in a balanced crossover design. During these protocols, either low sleep pressure conditions were attained by an alternating cycle of 150 min of wakefulness and 75 min of sleep (NAP) protocol, or high sleep pressure conditions were achieved by total sleep deprivation (SD) protocol. During scheduled wakefulness in both protocols, the PVT was carried out every 225 min. Quantitative analysis of the lapses, slowest (90th percentile) and fastest (10th percentile) reaction times (RTs) during the protocols, indicated that the lapses and slowest RTs were sensitive to changes in homeostatic sleep pressure. Our data indicate that the difference between the fastest and slowest RTs (interpercentile range 10th–90th percentile) was particular sensitive to detect very early effects of growing sleep pressure. On the other hand, decrements in PVT performance which were related to circadian phase did not depend significantly on any categorization (such as percentiles of the RTs).

© 2003 Elsevier Inc. All rights reserved.

Keywords: Neurobehavioral performance; PVT; Sleepiness; Sleep deprivation; Naps; Circadian rhythm; Homeostasis; Percentile

1. Introduction

Neurobehavioral performance (i.e., sustained attention) as assessed by the psychomotor vigilance task (PVT) exhibits a circadian modulation [1–4] and also reflects the effect of increasing sleep pressure with duration of time awake, without being confounded by a learning curve [2,5]. The modulations of neurobehavioral functions (e.g., cognitive throughput, short-term memory, alertness, and psychomotor vigilance performance) are best described by the two-process model of sleep–wake regulation [6,7]. A homeostatic process “S”, which increases exponentially with duration of prior wakefulness and decreases during sleep, interacts with a circadian process “C” driven by the biological clock to regulate the sleep–wake cycle. Recent investigations indicate that the interaction of these two processes is nonlinear for the prediction of waking neurobehavioural performance [8].

An experimental design that can partial out the contribution of these two major processes is the so-called forced desynchrony (FD) protocol. The FD protocol uses an imposed sleep–wake schedule outside the range of entrainment to the 24-h day (e.g., 28 h) to which the subject’s circadian pacemaker is unable to synchronize [9,10]. The constant routine protocol [11,12] provides the gold standard to measure endogenous circadian rhythms in physiological functions. In this protocol, however, certain measures such as self-rated sleepiness are masked by increasing sleep pressure during 40 h of sleep deprivation (SD) and the two processes “C” and “S” cannot be separated. We used a protocol that scheduled sleep at regular intervals during a 40-h episode so as to maintain low sleep pressure conditions and thus reveal the circadian rhythm of sleepiness without the confounding effects of elevated sleep pressure.

Of the metrics of the PVT, it is known that the lapses [reaction times (RTs)≥500 ms] and the 10% slowest RTs are sensitive to sleep pressure [4,13] but also to circadian time [14]. According to the ‘state instability’ hypothesis...
[15], neurobehavioral performance becomes increasingly variable under the influence of elevated sleep pressure due to inadvertent microsleep episodes, with brief moments of low arousal that make it difficult to sustain attention—a prerequisite for solving a vigilance task like the PVT. This unstable state, that fluctuates from second to second, is characterized by increased ‘lapses,’ more response errors, and increased compensatory efforts resulting in normal RTs for a short period of time (see Fig. 5 in Ref. [16]).

The aim of this study is to follow the time course of the neurobehavioral function during two protocols: an SD protocol and a nap (NAP) protocol both under constant routine conditions, so as to identify the effect of high sleep pressure (homeostatic process) versus low sleep pressure (circadian process) on the PVT. We expected, based on many empirical PVT results collected during SD, that the slowest RTs (lapses and 90th percentile of the RTs) would increase in the SD in contrast to the NAP. For the fastest RTs, we hypothesized that they will not be influenced by the applied sleep pressure conditions so that no significant difference between the protocols will be found. The reason for this prediction comes from the state instability concept: inadvertent microsleep episodes can be sufficiently compensated resulting in normal RTs for a short period of time and does not affect performance in the optimal domain (fastest RTs).

The homeostatic and the circadian processes represent an integral part of the regulation of brain activation and are also important in understanding the underlying mechanisms of neurobehavioral function (i.e., PVT performance). For applied research, which addresses the question of sustained attention (e.g., professional duties that demand high concentration and high accuracy), it is important to have a good objective and well-understood measure of vigilance to detect performance deficits as early as possible to prevent accidents.

2. Methods

2.1. Volunteers

Volunteers were recruited via poster advertisements at the University of Basel. After successfully passing a brief telephone screening, potential participants received detailed information on the study and three questionnaires: a morningness–eveningness-type questionnaire [17], the Pittsburgh Sleep Quality Index (PSQI [18]), and an extensive questionnaire covering sleep habits, sleep quality, life habits, physical health, and medical history. Subjects with self-reported sleep complaints (PSQI score >5) as well as extreme morning or evening types (score ≤12 or ≥23) were excluded from participation. Other exclusion criteria were chronic or current major medical illness or injury, smoking, medication or drug consumption, shift work within 3 months, or transmeridian travel within 1 month prior to the study.

Volunteers who did not fulfill any of the above exclusion criteria were interviewed and underwent a physical examination to exclude medical disorders. They spent an adaptation night in the laboratory to test their ability to sleep in a new environment and to exclude primary sleep disorders, e.g., sleep apnea. All participants gave signed informed consent, and the study protocol, screening questionnaires, and consent form were approved by the local ethical committee.

Sixteen healthy volunteers (8 male and 8 female, age range 20–31 years, mean=25.1, S.D.=3.4) were studied. Female participants started the study on Days 1–5 after menses onset in order to complete the entire study block within the follicular phase (four of the eight female participants used oral contraceptives). During the week preceding the study (baseline week), participants were instructed to maintain a regular sleep–wake schedule (bed and wake times within ±30 min of self-selected target time). The latter was verified by a wrist activity monitor (Cambridge Neurotechnologies, UK®) and sleep logs. They were also instructed to refrain from excessive physical activity, caffeine, and alcohol consumption. Drug-free status was verified upon admission via urine toxicologic analysis (DrugScreen Card Multi-6 for amphetamines, benzodiazepines, cocaine, methadone, opiates, and THC; von Minden, Germany). All participants completed the study without any complaints.

2.2. Design

Each participant underwent two study blocks (5 days each) with an off-protocol episode of 1–4 weeks (±2 weeks S.D.) in between, in a balanced crossover design (intra-subject comparison): a SD and a NAP protocol. They reported to the laboratory in the evening. The timing of the sleep–wake schedule was calculated in such a way that the 8-h sleep episode was centered at the midpoint of each participant’s habitual sleep episode as assessed by actigraphy during the baseline week. After a second 8-h sleep episode at their habitual bedtime (baseline night), a 40-h SD under constant routine conditions or a 40-h NAP protocol, both under constant posture conditions (near recumbent during wakefulness and supine during scheduled sleep episodes), was carried out (Fig. 1; for details of the protocol, see Ref. [19]). In the NAP, subjects completed 10 alternating cycles of 75 min of scheduled sleep and 150 min of scheduled wakefulness. The light levels were maximally 8 lx (typically 3–5 lx) during scheduled wakefulness and 0 lx during scheduled sleep. The protocol ended with an 8-h recovery sleep episode starting at habitual bedtime.

2.3. Psychomotor vigilance performance task

The PVT is a simple portable RT task to evaluate sustained attention [20]. The subject is instructed to press
a button as soon as the stimulus appears (LED-digital counter). In the present study, the duration of a single PVT trial comprised 5 min and the interstimulus interval varied randomly between 3 and 7 s. The PVT was assessed every 225 min starting 75 min after lights on in the morning (the first two PVT trials the day before the protocols served as training and were not analyzed), yielding 11 trials. During the NAP, the PVT was always scheduled 75 min before and after each nap.

2.4. Data analyses and statistics

The default performance metrics (e.g., mean of the RTs, response errors, lapses, i.e., RT≥500 ms; transformation by √x+√x+1; for details, see Ref. [21]) were delivered automatically by standard software (PVTcommW version 2.71/REACT version 1.1.03). We have analyzed the 10th and 90th percentiles of the distribution of the RTs, which provide a better measure than the mean of the 10%
slowest/fastest RTs—usually presented—which can be affected by extreme values. All PVT variables were first analyzed for order effects (whether participants completed the NAP or SD protocol first or vice versa) by ANOVAs for repeated measures (rANOVA). Thereafter, two-way rANOVAs were performed with the repeated factors 'type
of protocol’ (SD vs. NAP) and ‘time course’ (11 time points). All P values derived from rANOVA were based on Huynh–Feldt’s corrected degrees of freedom, but the original degrees of freedom are reported. Linear contrasts with the additional false discovery rate procedure for multiple comparisons [22] were performed to localize statistical differences between time points of SD and NAP.

3. Results

The distribution of the raw RTs for each PVT trial during the SD and NAP protocol is illustrated in Fig. 2 in order to show the impact of the protocols on changes in RT distribution. A comparison of the time course of the classical analysis (PVT lapses) and the extreme percentiles (10th and 90th percentiles) and their difference is shown in Fig. 3.

No significant order effect but a significant interaction between the ‘type of protocol’ and ‘time course’ was found for the following measures:

- The number of lapses were significantly more frequent in the SD protocol between 23.75 and 35 h into the protocol [interaction F(10,150)=2.7, P=.01; for post hoc comparisons, see Fig. 3a]. The number of lapses, which occurred at the very last time point, i.e., after 38.75 h into the protocol, was not significantly different between the SD and NAP protocol.
- The 90th percentile (slowest) of the RTs was significant slower between 23.75 and 38.75 h into the SD protocol [interaction F(10,150)=4.5, P<.001; for post hoc comparisons, see Fig. 3b]. The results for the 10% slowest RTs of the PVT metrics were similar and the time course had the same shape as the 90th percentile.
- The 10th percentile (fastest RTs) revealed no significant difference between the two protocols [interaction F(10,150)=1.7, P>.1]. However, the main effect ‘time course’ was significant [F(10,150)=3.3, P<.005]. The 10% fastest RTs of the PVT metrics showed the same results (data not shown).
- The difference of the 10th–90th percentiles (interpercentile range) of the RTs was significantly greater in the SD protocol between 20.00 h and 38.75 h [interaction F(10,150)=3.3, P<.005; for post hoc comparisons, see Fig. 3c].
- The response errors revealed no significant effect of the factors ‘type of protocol,’ ‘time course,’ and the interaction between these two factors.

4. Discussion

The main result of this study in regard to neurobehavioral performance is the different influence of increasing sleep pressure on the slowest (lapses and 90th percentile) and fastest (10th percentile) RTs measured by the PVT. In a protocol that augmented sleep pressure (SD), only the slowest RTs reflected this as a deterioration of psychomotor vigilance, whereas the fastest RTs were not affected. In contrast, in a protocol where the circadian process is prominent (NAP), the circadian modulation of the fastest and slowest RTs did not differ significantly.

Our results concerning the effect of growing sleep pressure on the lapse domain of the PVT (slowest RTs) confirmed the results shown in many studies looking at the effects of SD [5,13,14], which have been well demonstrated by Dinges and Kribbs (Fig. 4.1 in Ref. [23]) and Doran et al. (Fig. 5 in Ref. [16]) for a single time point during the day. Our study extends these analyses. We show the effect of circadian modulation in both low and high sleep pressure protocols first for the raw RT data distribution (Fig. 2) and second for the lapses and 10th and 90th percentiles of the RTs (Fig. 3). Fig. 2 gives a good visual impression of the development of the effect of low and high sleep pressure on PVT performance. Fig. 3 confirms previous findings that neurobehavioral functions remain stable for about 16 h of wakefulness under entrained conditions (e.g., Fig. 30.4 in Ref. [14]). Thereafter, lapses and the 90th percentile of the RTs undergo a clear circadian modulation with high values in the late night and early morning (deterioration of performance) and low values during the second day for both protocols. In addition, in the SD protocol, high sleep pressure is superimposed on the circadian modulation with maximum decrements after about 24 h of wakefulness, followed by a mild improvement during the second day of the protocol. Van Dongen and Dinges [14] described the effect of growing sleepiness during SD under controlled conditions (constant routine or under ambulatory experimental conditions) that “it is overlaid on an almost linear change reflecting increasing homeostatic pressure for sleep.” However, new investigations and studies of neurobehavioral functions using the FD protocol have shown that the interaction of the homeostatic and circadian processes is complex [8,14].

PVT lapses are—per definition—the slowest RTs of all. Therefore, the time course of PVT lapses is usually very similar to that of the slowest RTs percentiles (Fig. 3a and b). In many studies using the PVT under high sleep pressure, lapses have been established as one of the best metrics to show this effect [13,14,24–26]. We corroborate these results. PVT lapses were not significantly different after 38 h of SD compared with 38 h of sleep satiation. This final time point in our protocols coincides with the “wake maintenance zone” in the evening [27]. It may be that lapses in PVT performance, an objective measure of vigilance [23], are particularly sensitive to the circadian wake-promoting signal.

Concerning the fastest RTs (10th percentile of the RTs), our expectations were confirmed in regard to the ‘state instability’ hypothesis, that this domain of the RTs is not significantly influenced by sleep pressure, although a small
nonsignificant increase was visible on Day 2 of the SD protocol. In addition, a main effect of ‘time of day’ was present. If sleep pressure is considerably more augmented after longer deprivation of sleep than 40 h, it is evident that other metrics of the PVT will then also be affected, including deteriorations in the optimal domain [13,16,28].

Our expectations in respect to the lapse and optimal domain of the PVT performance were confirmed by the results predicted by the state instability hypothesis. According to this hypothesis, one would also expect an increase of the response errors during an unstable state of sustained attention under high sleep pressure as reported after 88 h of SD using a 10-min PVT test [16]. Our SD was only 40 h long and the duration of the PVT test session was reduced from 10 to 5 min. Both factors could explain our lack of finding an increase in response errors, which usually occur towards the end of the 10-min PVT sessions (Fig. 5 in Ref. [16]). It should be noted that in general, our subjects had a very low error rates (NAP: \( M = 2.1 \pm 0.5 \); SD: \( M = 1.9 \pm 0.4 \); mean values \( \pm S.D. \)), which may have contributed to the sustained good results even after 40 h of extended wakefulness.

The difference between the 10th and 90th percentile (interpercentile range) of the RTs can be considered as a reliable measure for the variability of the data. This range is significantly greater in SD compared with NAP. Interestingly, this measure showed a significant difference between SD and NAP after 20 h of prior wakefulness, which is 3.75 h earlier than the difference observed for the lapses and the 90th percentile of the RTs. It may be that the interpercentile range is an even more sensitive measure of the effects of growing sleep pressure on performance decrements than the lapses or the 90th percentile. However, this still needs a cross validation because of a possible type I error in the case of the difference measurement and of a type II error in the case of lapses and the 90th percentile.

The results of our study confirm the importance of circadian and homeostatic factors in the regulation of neurobehavioral function. For future studies, it will be important to characterize the interaction of these two factors in order to predict neurobehavioral performance based on sleep–wake history and circadian time.

Acknowledgements

This study was supported by Swiss National Foundation Grant START No. 3130-054991.98 and No. 3100-055385.98 to C.C. We thank C. Renz, M.-F. Dattler, and G. Balestrieri for their assistance in data acquisition.

References


