Reestablishment of individual sleep structure during a single 14-hour recovery sleep episode after 58 hours of wakefulness

Sleep before and after 58 h of wakefulness

Eva Hennecke[1], David Elmenhorst[2,3], Franco Mendolia[1], Matthias Putzke[1], Andreas Bauer[2,4], Daniel Aeschbach[1,5,6], Eva-Maria Elmenhorst[1,7]

[1] Institute of Aerospace Medicine, German Aerospace Center (DLR), 51170 Cologne, Germany
[2] Institute of Neuroscience and Medicine (INM-2), Forschungszentrum Jülich, 52425 Jülich, Germany
[3] Department of Psychiatry and Psychotherapy, Rheinische Friedrich-Wilhelms-University Bonn, Bonn, Germany
[4] Neurological Department, Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany
[5] Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, Boston, MA, 02115, USA
[6] Division of Sleep Medicine, Harvard Medical School, Boston, MA, 02115, USA
[7] Institute for Occupational and Social Medicine, Medical Faculty, RWTH Aachen University, 52074 Aachen, Germany

Author contributorship: D.E., A.B., D.A. and E.-M.E. designed research; E.H., D.E. and E.-M.E. performed research; E.H., F.M., M.P. & E.-M.E. analyzed data; E.H., D.A. and E.-M.E. wrote the paper; E.H., D.E., F.M., M.P., A.B., D.A. and E.-M.E. revised the paper

Number of words: 2220

Number of references: 14

All authors declared no conflicts of interest

Corresponding Author:

PD Dr. med. Eva-Maria Elmenhorst
DLR-Institute of Aerospace Medicine
Linder Höhe
51147 Köln
Germany

Phone: +49-(0)2203-6014735
Fax: +49-(0)2203-68323
Email: Eva-Maria.Elmenhorst@dlr.de

Summary

Sleep structure is highly stable within individuals but different between individuals. The present study investigated robustness of the individual sleep structure to extended total sleep deprivation. Seventeen healthy men spent a baseline night (23:00–7:00 h), 58 h of sleep deprivation and a 14-h recovery night (17:00–7:00 h) in the laboratory. Intraclass correlation coefficients (ICCs) showed that the agreement between baseline and recovery with respect to the proportion of the different sleep stages increased as a function of recovery sleep duration. High values were reached for most of the sleep stages at the end of 14 h of recovery sleep (ICCs between .38 - .76). If sleep duration of the recovery night is extended to 14 h, sleep stage distribution resembles that of a baseline night underlining the robustness of the individual sleep structure.

Introduction

Sleep loss necessitates a compensatory response during recovery sleep. According to the two-process model of sleep regulation (Borbely, 1982), a sleep deficit is not primarily recovered in duration but instead through increased sleep intensity. Sleep intensity is reflected in EEG slow wave activity (SWA; power density typically in the 0.75-4.5 Hz range), an indicator of homeostatic sleep pressure that is discharged according to an exponential function during undisturbed sleep. After a night without sleep, less than 10 h of recovery sleep are sufficient to reduce sleep pressure to a level that is typical for the end of an 8-h baseline sleep episode (Achermann and Borbely, 1994; Daan et al., 1984). However, SWA has been reported to be increased even during a second 10-h recovery night after sleep deprivation (Carskadon and Dement, 1985). Studies on cognitive performance before, during and after chronic sleep restriction suggested that homeostatic changes in sleep intensity cannot fully explain observed performance changes (Cohen et al., 2010). Taken together, it is still unknown, how much recovery sleep is truly needed to compensate for lost sleep.

Several studies have shown that sleep structure and in particular the distribution of sleep stages varies considerably among individuals, but is remarkably stable across nights within an individual (Buckelmüller et al., 2006). Even across nights interspersed with sleep deprivation, Tucker and colleagues (Tucker et al., 2007) found trait-like inter-individual differences in sleep parameters. Finelli and colleagues (Finelli et al., 2001) reported characteristic topographic power distributions in NREM sleep among individuals during a baseline night and a recovery night after 40 h of wakefulness.

It is currently unknown, to what extent sleep structure during extended recovery from sleep deprivation correlates with an individual's sleep structure under baseline conditions. Sleep deprivation can be viewed as a perturbation of an individual's trait-like sleep structure, and its reestablishment during recovery is expected to provide new insights into its robustness and into the time course of the recovery process. We therefore assessed the robustness of an individual's sleep structure across an interval of extended wakefulness (58 h) and determined whether/how quickly sleep structure reverts to baseline during a 14-h recovery sleep episode.

For our study design, the two-process model predicted that sleep pressure (process S) would already be reduced to baseline levels after 9.65 h of recovery sleep, while sleep duration would extend to 12.45 h because of the circadian influence (Achermann and Borbely, 1994; Daan et al., 1984). We hypothesized that an extension of sleep duration beyond 10 h is necessary to reestablish the individual sleep stage proportions, as the initial part of recovery

sleep is expected to be dominated by the homeostatic increase of N3 sleep at the expense of other sleep stages.

Methods

Participants

With ethical approval (ethics committee of the University of Düsseldorf) and written informed consent, 17 healthy men were included in the analysis (mean age 27 years, SD 5 years). Supporting Information (SI).

Design

The study design was described elsewhere (Elmenhorst et al., 2017). In brief, participants came to the laboratory for one adaptation night and one baseline night (23:00–7:00 h) before being sleep-deprived for 58 h. Finally, participants had a 14-h recovery night (17:00-7:00 h). Cognitive tests took place every 6 hours during baseline, during sleep deprivation and after recovery sleep.

Measurements

Sleep was measured by polysomnography. Sustained attention was tested with a Psychomotor Vigilance Task (PVT) (Elmenhorst et al., 2012). SI.

Data analysis

The proportion of sleep stages, as well as sleep onset latency (SOL), N3 latency, REM latency, and wake after sleep onset (WASO) were calculated. Within and between subjects variances as well as ICCs (absolute agreement) between nights were calculated on log-transformed sleep parameters and proportions (%) of the sleep stages after 6-14 h after sleep onset and interpreted according to Landis and Koch (Landis and Koch, 1977). Linear regressions were calculated on the ICCs for all sleep parameters. Sign tests compared the proportions of sleep stages after sleep onset during the baseline and recovery night. Based on Fast-Fourier Transformation (FFTs), SWA (1-4.5 Hz) in NREM sleep was calculated per 1.5-h intervals for baseline and recovery night and expressed as percentage of mean SWA in NREM during baseline night. PVT median reaction times were compared with Wilcoxon signed–rank tests during baseline, sleep deprivation and recovery (significance level was set at 0.025 according to Bonferroni). SI.

Results

The average proportion of Wake and the different sleep stages was similar for the 8-h baseline sleep episode and the 14-h recovery sleep episode (Table 1). The variance in sleep parameters between these two nights was greater between subjects than within subjects for all parameters but REM sleep, REM latency and N3 latency (Table 1). Moreover, the ICCs indicated substantial agreement (>0.6) for these variables on an individual basis except for REM sleep. The ICC values between baseline and recovery depended on the duration of the sleep interval included in the analysis (Fig. 1): if only the first 6, 7 or 8 hours were compared, the ICCs between baseline and recovery were relatively low. However, with every additional hour of recovery sleep included in the analysis the ICCs increased, i.e. the proportion of the sleep stages was more alike between the two sleep conditions. Linear regressions supported this observation for all sleep parameters but REM (Wake: $F_{(1,7)} = 49.33$, $p < .001$; N1: $F_{(1,7)} = 154.37$, $p < .001$; N2: $F_{(1,7)} = 16.91$, $p = .005$; N3: $F_{(1,7)} = 240.36$, $p < .001$; REM: $F_{(1,7)} = 5.52$, $p = .05$).

Fig. 2 indicates no further decrease in SWA after approximately 9-10 h of recovery sleep. Median reaction times increased significantly from 197 ms during baseline to 235 ms after 50 h of wakefulness ($Z = -3.52$; $p < .001$), whereas no difference ($Z = -.26$; $p = .81$) was found between baseline and recovery performance (200 ms).

Discussion

Robustness to experimental challenges has been postulated as representing one of the preeminent characteristics of traits (Van Dongen et al., 2005). Here, we compared individual sleep stage distribution before and after 58 h of total sleep deprivation in young, healthy men. It was found that even after such a large experimental challenge individual sleep stage distribution was remarkably robust, but only if a long enough recovery sleep interval (14 h) was considered. In fact, ICC agreement between the distribution of sleep stages in baseline and recovery sleep was low if only the first 6 h after sleep onset were considered, but increased steadily – except for REM sleep for which this pattern was less evident – with every additional hour of sleep beyond the first 6 hours. Thus, sleep parameters derived from the early part of a sleep episode are closely linked to state changes, whereas parameters that are based on the entirety of extended sleep appear to reveal underlying individual traits. Consistent with this conclusion, we found a low ICC for the sleep onset latency as well as the latencies to stage N3 and REMS, but high ICCs for the all-night proportions of the different sleep stages. The lower ICCs between the latencies and the sleep stage proportions after the

first hours of baseline and recovery night do not only express a lack of agreement of sleep parameter proportions within an individual, but also less variability between subjects due to similar recovery responses.

Previously, Tucker and colleagues (Tucker et al., 2007) showed trait-like inter-individual differences in sleep variables. They could establish robustness of inter-individual differences by examining eight nights interspersed with three separate episodes of sleep deprivation. Their results indicated greater inter-individual differences in sleep variables than group average effects in response to sleep deprivation. Our study focused on the reestablishment of individual sleep stage proportions after two nights without sleep. Robustness of the individual sleep stage distribution was found, but only when the recovery night was extended.

The reestablishment of individual sleep structure during extended recovery sleep may be an expression of ongoing – possibly homeostatic – recovery processes that are different from process S. In line with the calculations based on the two-process model, SWA reached asymptotic levels after approximately 9-10 h of recovery sleep in the present study. In contrast, our data on the reestablishment of individual sleep structure suggests that following 58 h of wakefulness recovery is not complete after 10 h of sleep. Protracted recovery responses have previously been reported for REM sleep (for review see: Aeschbach, 2011). However, the reestablishment of individual sleep structure is probably not only influenced by homeostatic processes, but also by the fact that the latter part of recovery sleep fell on the same circadian phase as the baseline sleep episode.

Our data suggest that recovery was sufficient after 14-h TIB. Firstly, the variance in sleep stages between total baseline and recovery night was greater between subjects than within subjects (except for REMS), indicating that the effect of sleep deprivation on sleep structure was smaller than the inter-individual differences in sleep physiology.

Finally, cognitive performance on the PVT was restored after 14-h recovery sleep. In a chronic sleep deprivation experiment, Banks and Dinges (Banks and Dinges, 2007) showed that PVT performance and slow wave energy were not restored to baseline levels after a single 10-h recovery sleep episode. Our data suggest sufficient recovery as indicated by performance assessment in the morning, but it remains unknown whether residual sleep loss effects may have affected performance and sleepiness later during the wake episode. (Cohen et al., 2010).

Our study has some limitations. Firstly, as pointed out before, the latter part of recovery sleep fell on the same circadian phase as baseline sleep, a fact that may have

contributed to the rising ICCs with increasing duration of recovery sleep, irrespective and independent of individual robustness of sleep. However, to assure that the results are not confounded by circadian timing, a study is needed where the latter part of recovery sleep falls at a different circadian time than the baseline sleep. Secondly, future studies could extend the duration of the experiment to clarify whether performance and sleep structure have been recovered or whether a further rebound is visible in a second recovery night.

In conclusion, the current study revealed remarkable robustness of individual sleep stage distribution to sleep deprivation, an observation that only became evident when considering a long enough recovery sleep episode. The finding substantiates the presence of strong underlying sleep traits. The reestablishment of an individual's sleep structure after sleep loss may offer a new perspective on the recovery process during sleep.

References

Achermann, P., Borbely, A.A. Simulation of daytime vigilance by the additive interaction of a homeostatic and a circadian process. *Biol. Cybern*, 1994; 71: 115-121.

Aeschbach, D. REM-sleep regulation: circadian, homeostatic, and non-REM sleep-dependent determinants. In: B. Mallick, S. Pandi-Perumal, R. McCarley, A. Morrison, (eds) *Rapid Eye Movement Sleep: Regulation and Function*. Cambridge University Press, Cambridge, 2011, 80–88.

Banks, S., Dinges, D.F. Behavioral and physiological consequences of sleep restriction. *J. Clin. Sleep Med.*, 2007; 3: 519-528.

Borbely, A.A. A two process model of sleep regulation. *Hum. Neurobiol*, 1982; 1: 195-204.

Buckelmüller, J., Landolt, H.P., Stassen, H.H., Achermann, P. Trait-like individual differences in the human sleep electroencephalogram. *Neuroscience*, 2006; 138: 351-356.

Carskadon, M.A., Dement, W.C. Sleep loss in elderly volunteers. *Sleep*, 1985; 8: 207-221.

Cohen, D.A., Wang, W., Wyatt, J.K. et al. Uncovering residual effects of chronic sleep loss on human performance. *Sci. Transl. Med.*, 2010; 2: 14ra3.

Daan, S., Beersma, D.G., Borbely, A.A. Timing of human sleep: recovery process gated by a circadian pacemaker. *Am. J. Physiol.*, 1984; 246: 161-183.

Elmenhorst, D., Elmenhorst, E.-M., Hennecke, E. et al. Recovery sleep after extended wakefulness restores elevated A1 adenosine receptor availability in the human brain. *Proc. Natl. Acad. Sci. U S A*, 2017; 114: 4243-4248.

Elmenhorst, E.-M., Rooney, D., Pennig, S., Vejvoda, M., Wenzel, J. Validating a 3-min psychomotor vigilance task for sleep loss-induced performance impairments. *J. Sleep Res.*, 2012; 21:115.

Finelli, L.A., Achermann, P., Borbely, A.A. Individual 'fingerprints' in human sleep EEG topography. *Neuropsychopharmacology*, 2001; 25: 57-62.

Landis, J.R., Koch, G.G. The measurement of observer agreement for categorical data. *Biometrics*, 1977; 33: 159-174.

Tucker, A.M., Dinges, D.F., Van Dongen, H.P. Trait interindividual differences in the sleep physiology of healthy young adults. *J. Sleep Res.*, 2007; 16: 170-180.

Van Dongen, H.P., Vitellaro, K.M., Dinges, D.F. Individual differences in adult human sleep and wakefulness: Leitmotif for a research agenda. Sleep, 2005; 28: 479-496.

Figure Legends

Figure 1: Intraclass correlation coefficients (ICCs) for the different sleep stage proportions in baseline and recovery sleep, plotted as a function of progressing recovery sleep: ICCs were calculated for different time intervals after sleep onset (i.e. first 6, 7, or 8 h after sleep onset in the baseline night correlated with first 6, 7, or 8 h of the recovery night and 8 h of the baseline night correlated with 9, 10, 11, 12, 13, or 14 h of recovery sleep).

Figure 2: Time course of SWA: The percentage of SWA in NREM during consecutive 1.5-h intervals of the baseline and the recovery night is expressed as the percentage of mean SWA during the baseline night. *: significant difference (Wilcoxon signed-rank tests) between % SWA of baseline and recovery, p-values were adjusted according to Bonferroni; grey diamond / black dot: individual data point baseline / recovery night.