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In search of objective components for sleep quality indexing in normal sleep☆

Roman Rosipal[a,b,*], Achim Lewandowski[a], Georg Dorffner[a]

[a] Section for Artificial Intelligence, Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Austria
[b] Department of Theoretical Methods, Institute of Measurement Science, Slovak Academy of Sciences, Slovak Republic

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ABSTRACT

The main goal of this study was to investigate to what extent polysomnographic (PSG) recordings of nocturnal human sleep can provide information about sleep quality in terms of correlation with a set of daytime measures. These measures were designed with the aim of comprising selected quality of night sleep and consist of subjective sleep quality ratings, neuropsychological tests and physiological parameters. First, a factor analysis model was applied to the large number of daytime measures of sleep quality in order to detect their latent structure. Secondly, in addition to the gold standard sleep staging method to arrive at variables about sleep architecture from PSG, we applied a recently developed continuous sleep representation by considering the probabilistic sleep model (PSM) describing the microstructure of sleep. Significant correlations between sleep architecture and daytime variables of sleep quality were found. Both the factor analysis and the PSM helped maximize the information about this relationship.

1. Introduction

How to define and objectively measure sleep quality is a long-term open question in sleep research. Usually sleep quality refers both to the subjective perception of sleep given by subjects via a standardized questionnaire, or a set of questionnaires, and to objective measures derived from physiological recordings (sleep architecture), most often from polysomnographic (PSG) recordings. The relation between such subjective and objective assessment of sleep quality is of great interest obviously leading to a better understanding of sleep. Available results indicate that subjectively rated sleep quality is usually correlated with periods of wakefulness during sleep time (sleep continuity), sleep latency, or with periods of slow-wave sleep corresponding to deep sleep (Åkerstedt, Hume, Minors, & Waterhouse, 1994, 1997; Keklund & Åkerstedt, 1997; Kryger, Steltjes, Pouliot, Neufeld, & Odynski, 1991; Saletu, 1975).

A different but not less important question is how sleep architecture relates to selected daytime quality of life measures, including cognitive, emotional, psychometric or physiological tests and measures. For example, does a poor or non-normal sleep profile necessarily mean impaired cognitive ability, increased sleepiness or reduced vigilance on the day following sleep? Different studies point toward some correlation between sleep architecture variables, such as sleep latency or total sleep time, and psychometric performance variables, such as reaction time (Yang, Lin, & Spielman, 2004) or physiological measures such as core temperature (Åkerstedt et al., 1997). To amplify this relationship it thus seems useful to search for the main dimensions reflecting different aspects of humans' quality of life influenced by sleep. Subsequently one can search for objective indicators extracted from the PSG recordings possessing a high level of correlation with the selected daytime measures of sleep quality.

The conventional description of sleep architecture from PSG recordings is carried out through applying the standardized Rechtschaffen and Kales (R&K) scoring manual (Rechtschaffen & Kales, 1968) or the recently published update of the rules (Iber, Ancoli-Israel, Chesson, & Quan, 2007).[1] The assignment of R&K sleep and wakefulness stages is based on electroencephalogram (EEG), eye movements (EOG) and muscle activity (EMG) recordings. According to the R&K manual, people usually pass through five stages of sleep: S1, S2, S3, S4, and REM (rapid eye movement) sleep. Stages S1–S4 are also known as non-REM (NREM) sleep. In this study stages S3 and S4 are considered as a single

* Corresponding author at: Dubravska cesta 9, 841 04 Bratislava, Slovak Republic. Tel.: +421 2 591 045 32.
E-mail address: roman.rosipal@savba.sk (R. Rosipal).

[1] While recognizing the existence of both rules sets for sleep staging that are currently followed in the sleep community, due to specific EEG montage recording protocol we focused on R&K labels only.

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sleep stage representing deep sleep also known as slow-wave sleep (SWS). However, the R&K sleep staging rules have been heavily criticized in the past and new ways of analyzing sleep have been discussed (Himanen & Hasan, 2000; Kubicki, Herrmann, & Höller, 1985; Schultz, 2008). According to Himanen and Hasan (2000) the major drawbacks of R&K are low temporal resolution, ignorance of spatial information, insufficient number of stages, and low correspondence between electrophysiological activity and stages. With the aim of avoiding these limitations an alternative computerized sleep model was introduced by the authors (Lewandowski, Rosipal, & Dorffner, 2012). The model, based on solid probabilistic principles, allows describing sleep on an arbitrarily fine time scale and allows considering sleep as a continuous process of transitions between a larger number of sleep sub-states (microstates) in contrast to the conventionally defined five sleep stages of R&K.

Using a large archival data collection of PSG recordings and daytime measures designed to comprehend selected aspects of sleep quality, the aim of the current study is to identify correlations between sleep architecture and the available daytime variables. To maximize the information contained in the data we apply two procedures. First, factor analysis is used to uncover the latent structure of a set of daytime variables such as subjective sleep quality, physiological and neuropsychological variables. These factors are then considered to represent new indexes of a subject's daytime physiological status and behavioral performance, supposedly influenced by sleep. The hypothesis that the factors would correlate better with sleep architecture is tested against the individual variables they consist of. Secondly, in addition to the gold standard R&K model of sleep architecture, we consider a continuous sleep representation by ways of the probabilistic sleep model (PSM) of Lewandowski et al. (2012). The PSM is an EEG data-based model of the sleep process represented by a number of different sleep microstates and a high time resolution allowing modeling of sleep microstructure. Microstates can be combined into subsets. This feature allows defining new sleep states or sub-states whose physiological interpretation and specific task-related performances can be studied. Using the model, a novel set of variables describing quantitative and qualitative characteristics of the probabilistic sleep profiles is extracted. The same procedure is repeated for the R&K sleep model. Both sleep-modeling approaches are validated with respect to their ability to reveal a maximum level of correlation between sleep architecture and the factors computed from daytime measures of sleep quality.

2. Materials and methods

2.1. Subjects and study design

Data of 148 subjects (67 males and 81 females), age between 20 and 86 (mean 51 years and standard deviation 20 years), from the sleep database created during the EU SIESTA project (1997–2000) were used (Klösch et al., 2001).[2] One aim of the SIESTA project was to create a normative database of disorder healthy and sleep-disturbed patients. The project was organized as a multicenter study, which comprised eight clinical partners and eight engineering groups located in Europe. According to the SIESTA recording protocol all subjects had to document their sleep habits over 14 nights. Subjects spent two consecutive nights (7th and 8th night) in the sleep laboratory during which PSG recordings were obtained. Therefore, 296 all-night PSG recordings were used in this study. PSG recordings started at the subjects' usual bedtime and were terminated at their usual time of getting up in the morning. Within the SIESTA project the ICD-10-based (World Health Organization, 1992) diagnosis was used to identify subjects with sleep related disorders including sleep apnea, nonorganic insomnia, mild to moderate generalized anxiety disorder, mood disorder, Parkinson's disease, and periodic limb movement disorder (Klösch et al., 2001) and these patients were not used in the current study. Subjects with a history of drug abuse or habituation (including alcohol), subjects requiring psychoactive medication and/or other drugs that might interfere with the SIESTA study assessments, subjects who were unable or unwilling to comply with the protocol, and subjects working at night were not included. Finally, only subjects without significant medical disorders interfering with the aim of the SIESTA study (Klösch et al., 2001), with a Mini Mental State Examination score $\geq$25 (Folstein, Folstein, & McHugh, 1975), a Pittsburgh Sleep Quality Index global score $\leq$ 5 (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989), a Self Rating Anxiety Scale score < 33 (Zung, 1971), a Self Rating Depression Scale score < 35 (Zung, 1965), and with a bedtime between 22:00 and 24:00 were considered in this study. Considering R&K scoring, the average values of selected sleep parameters and the average percentages of sleep stages are summarized in Table 1.

Table 1
Average values of selected sleep parameters and the average percentages of sleep stages computed with respect to the total sleep time. Values represent averages computed by considering the R&K hypnograms of 148 subjects. NASO - number of awakenings after sleep onset, WASO - wakefulness after sleep onset.

	Night 1	Night 2
Total time in bad (h)	7.9	7.9
Total sleep time (h)	6.4	6.8
Sleep latency (min)	23	17
Sleep latency to REM (h)	2.3	1.7
NASO	19	17
WASO (min)	62	45
Sleep efficiency (%)	81	86
S1 (%)	10	9
S2 (%)	57	55
SWS (%)	15	15
REM (%)	18	21
Number of REM cycles	3.3	3.8

The PSG recording protocol specified 16 channels of biosignals: 6 EEG channels with mastoid as reference (Fp1-M2, C3-M2, O1-M2, Fp2-M1, C4-M1, and O2-M1), an additional EEG channel (M1–M2) for re-referencing, 2 EOG channels, submental EMG and EMG recorded from electrodes placed at the musculus anterior tibialis of the left and right leg (electrodes were linked), electrocardiogram and respiratory signals (airflow; movements of the chest wall and abdomen and O_2 saturation of arterial blood).

During the stay in the sleep laboratory subjects performed several neuropsychologic tests for assessment of attention, attention variability, concentration, short-term memory, fine motor activity and drive (Table 2). The test results used in this study were carried out under strictly the same conditions in the morning after sleep. Tests were carried out after washing, getting dressed and breakfast and in general between 1 and 2 h after getting up. Evening blood pressure and pulse values were recorded less than 2 h before bedtime and in the morning after sleep. After sleep all subjects filled out several questionnaires monitoring and scoring their subjective sleep and awakening quality. Subjective sleep and awakening quality was assessed in the morning utilizing a standardized Self-rating Scale (SSA; Saletu, Wessely, Grünberger, & Schultes, 1987). The SSA consists of 20 items and yields three sub-scores (sleep quality, awakening quality and somatic complaints) as well as a total score (Table 3). Four 100 mm visual analog scales (VAS; Aitken, 1969) for drive, mood, affectivity and drowsiness were also used. The self-assessment questionnaire of well-being consisting of 28 items (von Zerssen, Köller, & Rey, 1970) was filled by subjects in the evening and morning sessions. Tests are summarized in Table 4.

2.2. Daytime variables processing – factor analysis model

The aim of using the factor analysis (FA) model was to describe variability among the measured daytime variables (Table 4) through a set of fewer unobserved variables, called factors. The observed variables can be modeled as linear combinations of the factors and error terms,

$$\mathbf{x} = \mathbf{\Lambda f} + \boldsymbol{\varepsilon}$$

where $\mathbf{x}$ is a vector of zero-mean (centered) observed variables, $\mathbf{\Lambda}$ is a constant matrix of factor loadings, $\mathbf{f}$ is a vector of independent, standardized common factors, and $\boldsymbol{\varepsilon}$ is a vector of independent specific factors, error terms. In this study the maximum likelihood estimate of the factor loadings matrix $\mathbf{\Lambda}$ was used (Gorsuch, 1983). The *varimax* rotation was used to rotate the estimated factor loadings. Finally, the Bartlett method was applied to estimate the factor scores (Gorsuch, 1983). The method allows expressing each factor score as a linear combination of the observed variables. Therefore for each subject and each factor, two factor scores (two values) can be computed using the set of variables collected during two days the subjects spent in the sleep laboratory.

2.3. Sleep modeling and sleep parameters extraction

We used two different approaches of modeling the sleep process: i) the traditional R&K modeling of the sleep based on the discrete staging, and ii) the novel

[2] The complete dataset consists of 175 healthy normal sleep subjects. In this study we excluded 27 subjects from the same sleep center due to inconsistent observed values of several daytime physiological variables.

Table 2
Neuropsychological tests description.

Numerical memory test Grünberger (1977)	Short-term memory test *Task: The test consists of two parts*: *1st part – seven rows of three to nine digits must be memorized forward* *2nd part – seven rows of two to eight digits must be memorized backward*
Alphabetical cross-out test Grünberger (1977)	Paper pencil test (speed test) for quantification of attention, concentration and attention variability *Task: The subject has to cross-out letters from a combination. For each column the subject has 10 s and he is instructed to work as fast as possible. For evaluation of attention the total score, for measurement of concentration the percentage of errors, and for the determination of attention variability the difference between extreme scores, is used*
Fine motor activity test Grünberger (1977)	Paper pencil test (speed test) for evaluation of changes in psychomotor activity and drive (left and right hand) *Task: The subject has to set dots in boxes (1.0 × 0.5 cm) within 15 s, first with the right and then with the left hand. The sum of the dots from both sides is a measure of motor activity and drive*

Table 3
Self-rating Questionnaire for Sleep Quality, Awakening Quality and Somatic Complaints (Saletu et al., 1987). Four possible answers ('no', 'slightly', 'moderately', and 'very much') are associated with each question. The answers are quantized and a single score value is computed.

Sleep quality (ssq)	Awakening quality	Somatic complaints
1. Did you sleep well?	8. Did you feel giddy after awakening?	16. Any nausea after awakening?
2. Did you have deep sleep?	9. Did you feel disoriented?	17. Any headache?
3. Did you have difficulties in falling asleep?	10. Did you feel tired?	18. Dryness of your mouth?
4. Did you have difficulties in staying asleep?	11. Were you in a good mood?	19. Any dizziness?
5. Did you have bad dreams?	12. Did you feel interested in your surroundings?	20. Incoordination of movements?
6. Did you have difficulties getting back to sleep?	13. Did you feel slowed down?	
7. Did you wake up earlier than usual?	14. Was your attention/concentration reduced?	
	15. Did you feel refreshed and rested?	

Table 4
Factor loadings for the first three factors computed from daytime variables defined in the first column of the table. Dominant loading values for each factor are shown in bold.

Observed variables	Factor 1	Factor 2	Factor 3
Self-rating Questionnaire for Sleep Quality (ssq)	**+0.24**	+0.10	−0.00
Self-rating Questionnaire for Awakening Quality	**+0.54**	+0.07	−0.09
Self-rating Questionnaire for Somatic Complaints	**+0.28**	+0.20	−0.00
Numerical Memory Test	−0.01	−0.23	**+0.41**
Well-being Self Assessment Scale (evening)	**+0.44**	−0.06	+0.10
Well-being Self Assessment Scale	**+0.70**	−0.01	+0.11
Pulse Rate	−0.09	−0.07	−0.12
Pulse Rate (evening)	−0.19	−0.11	−0.04
Systolic Blood Pressure	+0.06	**+0.85**	−0.17
Systolic Blood Pressure (evening)	−0.04	**+0.84**	−0.20
Diastolic Blood Pressure	+0.12	**+0.72**	−0.13
Diastolic Blood Pressure (evening)	+0.02	**+0.70**	−0.07
Visual Analog Scale Test for Drive	**+0.84**	−0.00	+0.02
Visual Analog Scale Test for Mood	**−0.75**	+0.03	+0.01
Visual Analog Scale Test for Affectivity	**−0.73**	+0.01	+0.15
Visual Analog Scale Test for Drowsiness	**+0.81**	−0.10	+0.07
Alphabetical Cross-out Test (total score)	−0.04	−0.19	**+0.52**
Alphabetical Cross-out Test (variability)	+0.09	−0.03	−0.02
Alphabetical Cross-out Test (% of errors)	+0.01	−0.03	−0.01
Fine Motor Activity Test (right hand)	−0.05	−0.19	**+0.93**
Fine Motor Activity Test (left hand)	−0.01	−0.12	**+0.83**
Explained variance	17.4%	12.6%	10.3%

probabilistic sleep model treating the sleep as a continuum with a higher number of sleep microstates. However, the aim of the study is not testing one model against the other but to investigate differences between the extracted sleep parameters from both models by examining how these sleep parameters correlate with the measured daytime variables or computed factor scores.

2.3.1. Rechtschaffen & Kales sleep model

The sleep structure was analyzed in 30 s epochs according to the standard R&K scoring rules for sleep staging (Rechtschaffen & Kales, 1968). To this aim, the computerized system Somnolyzer 24 × 7 (Philips-Respironics) was used (Anderer et al., 2005). To assign the wakefulness periods, REM and NREM sleep stages, the system uses information from EEG, EMG, EOG and respiratory channels. Data from the C3-M2 EEG channel were used. If artifacts occurred the channel was replaced by C4-M1. EEG segments, for which both channels show artifacts, were ignored. The artifact detection procedure of the Somnolyzer 24 × 7 was applied for detecting eye, muscle, sweat and EEG amplitude related artifacts. The system includes a quality review process that only takes some minutes of a human expert's time. Somnolyzer 24 × 7 is a thoroughly validated computer supported sleep scoring system deriving from PSG recordings a sleep profile (hypnogram) and all related events (Anderer et al., 2005, 2010).

The extracted hypnograms were consequently analyzed and 110 sleep parameters were computed. These parameters include sleep characteristics such as total time in bed, total sleep time, sleep efficiency, wakefulness during total sleep period, relative and absolute time during individual sleep stages, latencies to sleep stages, number of sleep stage changes, number of awakenings, number and average duration of REM and NREM cycles. In addition, the whole time in bed period was divided into quarters and relevant sleep parameters were computed for each time quarter separately. Having 148 subjects and considering each of the two nights PSG separately 296 values of each sleep parameter were computed. Subsequently, Spearman rank correlation coefficients were computed between each sleep parameter and each daytime variable as well as each of the three considered factor scores (Table 4).

With aging, sleep profiles tend to change (Vitiello, 2006). The same is true for some daytime measures. When a statistically significant correlation between age and a given variable was observed, we compensated the effect by detrending using a second order polynomial fit.

2.3.2. Probabilistic sleep model

A new probabilistic sleep model (PSM) proposed by the authors was used to represent sleep as a continuum (Lewandowski et al., 2012). The current version of the model uses data from EEG recordings only. In the same way as in the case of the R&K model, the C3-M2 (or alternative C4-M1) EEG channel and the same artifact detection procedure were used. The model creates a sleep profile via posterior probabilities of a finite number of sleep substates – called microstates – not necessarily reflecting the structure of the R&K stages (Fig. 1). In the used version of the PSM posterior values were computed for every 3 s long non-overlapping data window (Lewandowski et al., 2012). The number of microstates is derived from the observed sensor data itself using an appropriately selected model criterion. In the study the PSM with 20 microstates and the same additional PSM parameters and data setting as described in Lewandowski et al. (2012) was considered. Microstates can be combined into subsets and their physiological interpretation and a specific task related performance can be studied. By considering data periods with R&K staging labels, probabilities of each microstate toward each of the five standardized stages can be determined during the training process and a R&K-like sleep structure can be derived (Fig. 2).

Considering each subject and each night the PSM sleep profiles were constructed (296 sleep profiles; 148 subjects and 2 nights for each). From each profile 268 sleep parameters were computed and correlated with the factors scores and daytime variables (Table 4). These sleep parameters can be divided into two categories. First, the R&K like probabilistic sleep profiles can be constructed (see Fig. 2). At each time point a maximum posterior value can be selected and a corresponding R&K sleep stage can be assigned. In this way continuous sleep profiles can be discretized into a single R&K hypnogram and sleep parameters described in the previous sub-section can be computed. Note that this is done on a 3 s long basis in contrast to the 30 s long R&K staging. Second, posterior probability curves of microstates and their combination can be used to extract novel sleep parameters specific for this form of sleep modeling. Two measures are in the focus of this paper. First, it is the area under the curve (AUC). In this study the AUC of the original values and absolute values of the

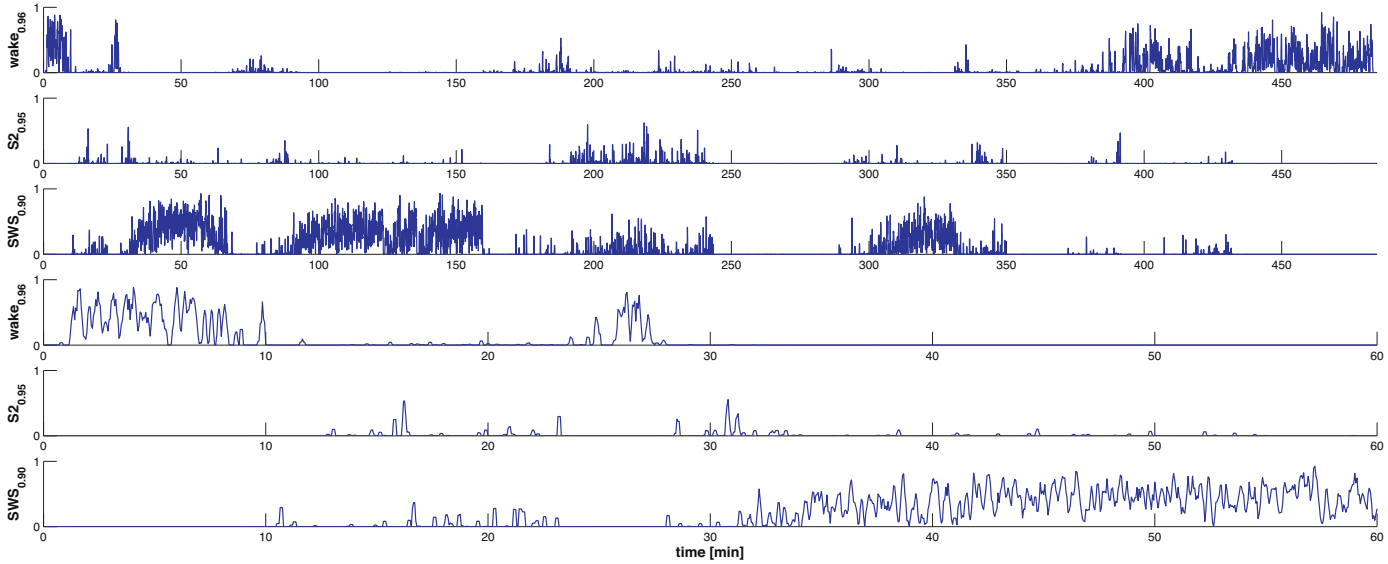

Fig. 1. An example of smooth posterior probability values of three sleep microstates (microstate sleep profiles) for a 32 years old male. The probabilistic sleep model used in this study consists of 20 microstates. Using the R&K labels (or their subset) a vector of probabilities (weights) summing up to one can be estimated and connected to each microstate. This vector expresses the contribution of a microstate to each of the R&K sleep stages. This allows combining all (or a subset of) microstates, and a sleep profile mimicking the R&K like structure can be constructed (see Fig. 2). *Top three plots*: Whole night sleep profiles for microstates with the strongest weight toward wake (weight value for the R&K wake stage equal to 0.96), S2 (weight value for the R&K S2 stage equal to 0.95) and slow-wave sleep (SWS, weight value for the R&K SWS stage equal to 0.9). *Bottom three plots*: Detailed plots of the top three plots depicting the first hour of sleep. For visualization purposes the posterior curves were smoothed with moving average over 9 s.

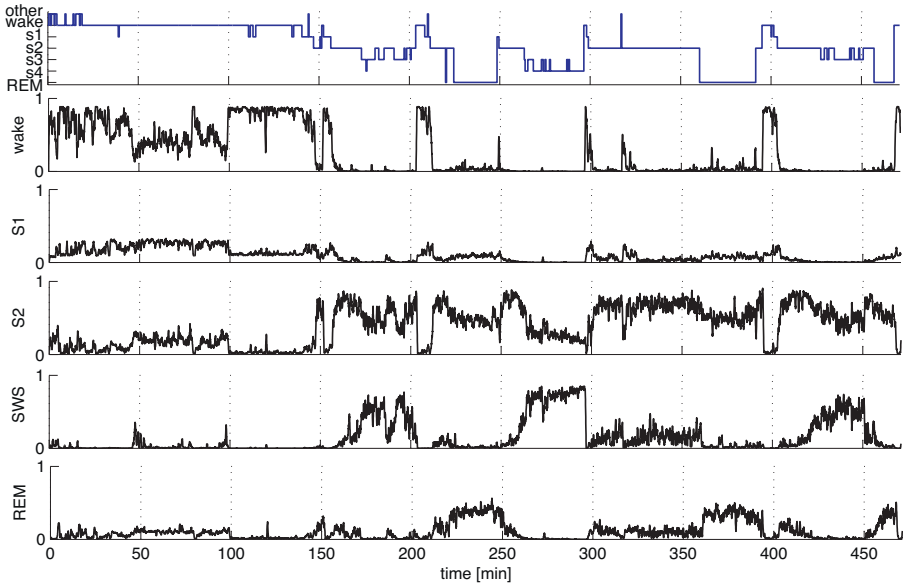

Fig. 2. An example of the all-night R&K and PSM sleep profiles for a 41 years old female subject. The R&K hypnogram is presented at the top. Posterior probability curves of the PSM reflecting R&K staging are depicted in the second to sixth subplots from the top (wake, S1, S2, slow-wave sleep (SWS) & REM). Every PSM curve represents posterior values after combining 20 microstates of the PSM. For visualization purposes the posterior curves were smoothed with moving average over 30 s.

first and second derivatives of the probability curves were computed. However, a high similarity between the results of the individual AUC-based sleep parameters was observed and for clarity of the presented results all are denoted as the AUC and are not further distinguished. The second specific PSM measure is an analogy to the so-called spectral entropy (Inouye et al., 1991). Probability curves were normalized with respect to time resulting in a sample probability density function for which the Shannon entropy was computed. In the context of the current research, such an entropic measure can be understood as a measure differentiating curves of different patterns in the following way. Curves with a single or few distinct peaks will be represented by low values, while curves with a flat probability profile over the investigated time period will be represented by the highest values of this entropic measure. Therefore the measure can be a good indicator of probabilistic curves with different types of patterns driven by the existence of longer and shorter peaks.

The PSM sleep parameters AUC and entropy can be computed from the posterior probability values of each sleep microstate separately. In addition these sleep parameters can also be computed by considering an arbitrary combination of microstates in a way that such combinations will not necessarily represent the R&K structure of sleep stages. The simplest example can be sleep parameters computed from a single raw microstate.

The age effect was compensated in the same way as in the case of the R&K model.

3. Results

3.1. Three factor scores

Using the varimax rotation three dominant factors were extracted from daytime variables (Table 4, the first column). These factors described 40.3% of the overall data variance in the

original space of the observed daytime variables. The percentages of the variance described by the individual factors were 17.4%, 12.6%, and 10.3%, respectively. Factor loadings for each factor are shown in Table 4. Dominant loading values shown in bold suggest the following interpretation of the factors. The first factor represents subjective quality of night sleep defined through a set of visual analog scale (VAS) variables and the used questionnaires. The physiological measures of blood pressure have the highest weighting in the case of the second factor. Therefore this factor can be understood as the *physiological* factor reflecting a subset of the observed physiological measures. Finally, the neuropsychological test variables are dominant elements building up the third factor. Subsequently, this factor will be referred to as the *neuropsychological* factor.

Computing the FA model with more than three factors resulted in the atomization of the loading structure of the first three factors; that is, factors with high loadings for a single or few observed variables were observed. For example, the fourth atom was characterized by dominant loadings for morning and evening pulse variables and accounted for 6% of the overall variance. These further factors were not considered in this study.

3.2. Correlations with factor scores

Spearman rank correlation coefficients between the extracted sleep parameters and factor scores were computed. These values were compared with the correlation coefficients computed between sleep parameters and standalone subjective sleep quality, physiological and neuropsychological variables (Table 4). Sleep parameters from both PSM and R&K models were used. The aim of this comparison was to show that the extracted three factors provide a comparable or higher degree of correlation with the sleep parameters and therefore the factors can replace individual variables they consist of. A one-sided two-sample t-test (significance level $\alpha = 0.01$) was used to test the null hypothesis about the difference in means of the absolute value correlation coefficients computed either for individual daytime variables or for the three factor scores. First, it was observed that the Self-rating Questionnaire for Sleep Quality scores (henceforth denoted as *ssq*; Table 3, the first column) alone show the significantly higher mean value of correlation with the R&K and PSM sleep parameters in comparison to the first factor score. This indicates that for the purposes of this study the first factor is not a good replacement of subjective sleep quality variables. Therefore the *ssq* variable alone was used instead. However, opposite results were found for the second and the third factor. In these cases the correlation coefficient means for both factor scores were significantly higher or statistically not different in comparison to the correlation means computed for individual variables with the highest loadings (Table 4, bold values). Therefore the second and third factors were used to represent daytime physiological and neuropsychological aspects of subjects related to night sleep.

3.3. Age effect

To test the influence of age on the Self-rating Questionnaire for Sleep Quality the correlation between the *age* and *ssq* variables was computed. The Spearman correlation coefficient ρ was equal to 0.04 and the effect was not statistically significant ($p = 0.46$).[3] However, a significant age dependence was found for the second and the third factor ($\rho = 0.43$, $p < 0.01$; $\rho = -0.54$, $p < 0.01$); see Fig. 3. Interestingly, Fig. 3 also indicates that the age dependence is low or negligible for ages below 40 years. The influence of age increases for subjects older than 40 years. By selecting the subjects younger than 40 years the same test about significant correlation between the *age* variable and the two factors was applied. Now, for both factors no significant correlations were found ($\rho = 0.01$, $p = 0.92$; $\rho = -0.09$, $p = 0.36$). Two other ways of subjects' grouping were considered and the same dependence of the factor scores on age was investigated. We defined a middle age group (40–60 years) and an elderly people group ($\geq$60 years). The middle age group showed significant correlations for both factors ($\rho = 0.33$, $p < 0.01$, $\rho = -0.23$, $p = 0.03$). For the elderly people significant correlations were found for the third factor ($\rho = -0.25$, $p = 0.01$) but not for the second factor, where the correlation coefficient was different from zero but not significant ($\rho = 0.12$, $p = 0.22$). Therefore, the age effect was corrected in the following way. If a significant correlation (significance level $\alpha = 0.05$) was observed between age and an investigated variable, the effect was compensated by subtracting a second order polynomial fitted to the data in a least square sense. This was done for every factor score and every sleep parameter showing significant age effect. In addition, subjects younger than 40 years (48 subjects) were considered separately and the subsequent analysis was carried out without correcting the factor score values (sleep parameters with significant age effect were corrected). Note, similar to the result obtained for the whole set of subjects, no significant correlation between the *age* and *ssq* variables was found for this group ($\rho = 0.03$, $p = 0.77$).

3.4. R&K and PSM

Table 5 summarizes the highest statistically significant ($\alpha = 0.01$) Spearman rank correlations between the R&K sleep parameters and the three variables: *ssq*, physiological factor score and neuropsychological factor score. Sleep parameters are grouped by sleep stages but also general sleep parameters (GSP) are used. The parameters are either normalized by considering two different time periods; time in bed (*tib*) and total sleep time (*tst*), or absolute times (*at*) spent in particular sleep stages are considered. In addition four periods dividing the overall time in bed into quarters are considered (*q1–q4*). The notation of Table 5 can be explained by the following example. Consider the *q3/rtst* sleep parameter belonging to sleep stage S1. The parameter represents the duration of S1 sleep during the third quarter of the night normalized by the total sleep time during this quarter.

It can be observed that *ssq* shows the highest correlation with the wake related sleep parameters and similarly shows a significant, negative correlation with sleep efficiency. The second and third quarters of the night seem to be the most important periods to monitor this relation. Note that the negative values of the correlation reflect the fact that small values of *ssq* represent good sleep. Only few sleep parameters showed a significant correlation with the physiological factor. The highest correlation can be found between the sleep parameters associated with wakefulness during the third quarter of the night and SWS during the second quarter of the night. The R&K sleep parameters showed no significant correlations with the third, neuropsychological, factor.

Similarly to Table 5, statistically significant Spearman rank correlations for the PSM are shown in Table 6. In addition to the sleep parameters used in Table 5, the sleep parameters representing the specific aspects of the individual sleep stage posterior value profiles were computed. These are the area under the curve (*auc*) and entropy (*ent*). In comparison to the R&K model, similar correlation values for *ssq* can be observed for the wake and sleep efficiency parameters. However, in contrast to the R&K sleep parameters, the *auc* and *ent* sleep parameters computed for the S2 and SWS stages show higher correlations indicating the importance of these sleep stages for subjective sleep quality monitoring. In contrast to the R&K sleep parameters, the PSM provides a set of parameters

[3] On the same SIESTA database, Saletu et al. (2005) found that the self-rating questionnaire for sleep and awakening quality tests are not influenced by age.

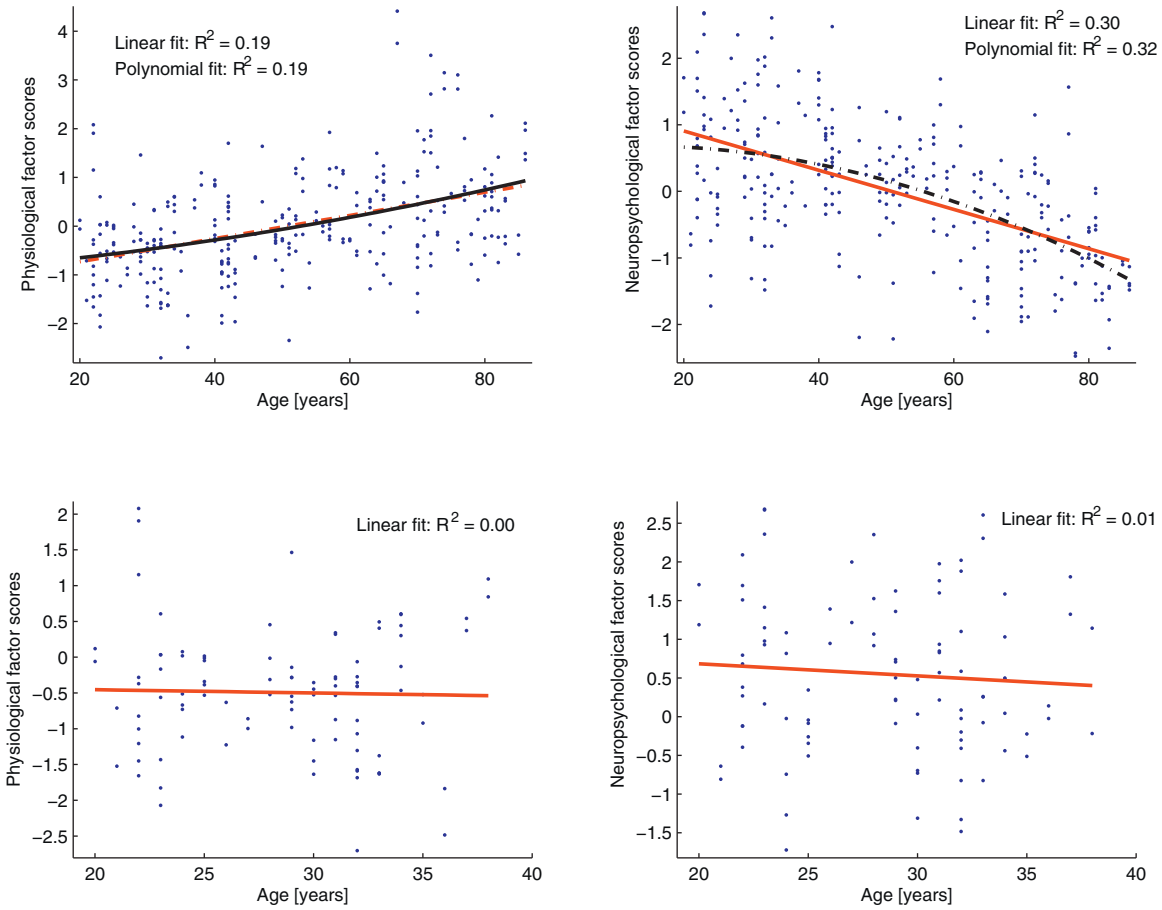

Fig. 3. Effect of age in the case of physiological (left plots) and neuropsychological (right plots) factors. Linear (solid line) and the second order polynomial (dash-dotted line) fits to the data are also depicted. Top plots (all subjects): Spearman rank correlation with age: 0.43 physiological factor; −0.54 neuropsychological factor. Bottom plots (young subjects; <40 years): Spearman rank correlation with age: 0.01 physiological factor; −0.09 neuropsychological factor. R^2 denotes the coefficient of determination.

showing a higher level of correlations with both physiological and neuropsychological factors almost for all sleep stages. Significant correlation values for the sleep parameters computed for all three sleep stages (S1, S2 and SWS) can be observed. In addition, the PSM sleep parameters computed for wake and REM show significant correlations with the physiological factor. Note that, although statistically significant, the correlations computed for the second and third factors are small in absolute values. Next, the same analysis was carried out for young subjects (<40 years old, 48 subjects). The results are summarized in Table 7. Now, correlations with higher absolute values can be observed for the second and third factors. For the second factor, significant positive correlations with wake and S1 sleep parameters, in contrast to the negative correlations for S2 and SWS, indicate that sleep with higher wakefulness and less SWS positively correlates with higher blood pressure values. The last column of Table 7 shows that neuropsychological test performance is positively correlated with the higher amount of sleep in REM and negatively with the amount of SWS mainly during the third and fourth quarters of the night.

3.5. Beyond R&K

The PSM allows combining sleep microstates into subsets and thus creating different sleep profile – structures. The following strategy of combining sleep microstates was used in the study. A vector of probabilities summing up to one is connected to each microstate. This vector expresses the contribution of a microstate to each of the R&K sleep stages. Separately considering each element of this vector, combinations of microstates were created. For each element, the maximum probability value among all microstates was found. Then, only microstates with values greater than 10% of this maximum value were combined. Finally, the combinations of microstates with the highest values of correlation were selected. To keep robustness of such a selection the bootstrap method (drawing with replacement) was used to generate a training set. The size of the training set was set to the half of the number of all considered subjects. The PSM was re-trained with the new training set and the sleep parameters from all possible combinations of microstates were computed. Sleep parameters showing the highest correlation values were selected and computed again using the test set consisting of all subjects. The procedure was repeated 50 times and only sleep parameters with statistically significant correlation values observed in more than 40 runs are reported.

Results for young subjects are summarized in Table 8. In comparison to Table 7 similar or usually slightly higher correlation values of the *auc* and *ent* sleep parameters can be observed. In contrast to Table 7 where the sleep parameters for each sleep stage were computed using the full set of 20 sleep microstates, now the average size of the combined microstates is smaller (Table 8, values in brackets). This finding indicates that changes in substructures of the traditional R&K sleep stages may better reflect important aspects of sleep that are related to daytime subjective or objective evaluation of night sleep quality.

4. Discussion

The factor analysis of 21 variables monitoring different subjective and objective aspects of subjects' daytime quality of life status

Table 5
Statistically significant ($\alpha = 0.01$) Spearman rank correlations (ρ) between the R&K sleep parameters and three variables representing subjective sleep quality (*ssq*), physiological test results (factor score 2) and neuropsychological test results (factor score 3). Statistically significant correlation values after Bonferroni correction are in bold. Abbreviations: S1–S4, sleep stages; S34, slow-wave sleep (S3 + S4); GSP, general sleep parameters; q1–q4, four equal quarters of tib, where tib stands for time in bed (time starting from lights-off until lights on); tst, total sleep time (sum of time in the sleep stages S1–S4 and REM); rtst, relative values normalized by tst; at, absolute time; atsp, absolute time within tsp, where tsp stands for total sleep period (time from the first appearance of any sleep stage until final awakening); eff, sleep efficiency, tst/tib; slat, sleep latency to a sleep stage; fw, number of awaking during tsp; n-nremc, number of NREM cycles, a-nrems, average duration of NREM cycles, fs, number of sleep stage changes during tsp.

Sleep stage	ssq subjective sleep quality		Factor 2 physiological		Factor 3 neuropsychological	
	Sleep par.	ρ	Sleep par.	ρ	Sleep par.	ρ
Wake	at	**0.37**	q3/at	0.19		
	atsp	**0.37**	q3/atsp	0.19		
	q2/at	**0.31**	at	0.18		
	q2/atsp	**0.31**	atsp	0.18		
	q1/at	**0.24**				
	q3/at	**0.24**				
	q3/atsp	**0.24**				
	q4/at	0.19				
	q1/atsp	0.19				
S1	slat	0.19	q3/rtst	0.17		
	q1/rtst	0.16	q3/at	0.16		
	rtst	0.15				
S2	slat	0.19				
S3, S4			q2/at	−0.16		
			q2/rtst	−0.16		
REM	at	**−0.25**				
	slat	0.21				
	q2/at	−0.20				
	q3/at	−0.18				
	rtst	−0.16				
	q2/rtst	−0.15				
GSP	eff	**−0.36**	q3/eff	−0.19		
	q2/eff	**−0.31**	q3/fw	0.19		
	tst	**−0.27**	fw	0.18		
	q2/tst	**−0.25**	eff	−0.17		
	q3/eff	**−0.24**				
	q3/eff	**−0.24**				
	q3/fw	**0.23**				
	q2/fw	0.22				
	fw	0.22				
	q1/tst	−0.19				

revealed three dominant factors. These factors clearly grouped variables reflecting subjective sleep quality, physiological measures and neuropsychological test results. Factors with the same underlying structure were also observed after grouping the subjects into three different sets according to their age ([20,40), [40,60), and ≥60). A sufficiently high number of subjects should guarantee stable interpretation of the factors.

The first factor representing subjective sleep quality turned out not to be as highly correlated with the R&K and PSM sleep parameters as the *ssq* variable alone. Significant, but only moderate correlations between *ssq* and the R&K sleep parameters were reported in the previous studies (Saletu et al., 2005). These results correspond to the findings in the current study where sleep efficiency, total sleep time, wakefulness and number of awakenings during total time in bed or total sleep period are the sleep parameters showing the highest correlations. A connection between perceived sleep quality and sleep efficiency or total sleep time was also found by Keklund and Åkerstedt (1997) and Åkerstedt et al. (1994). Considering a sleep-quality index related to the initiation and maintenance of sleep, Keklund and Åkerstedt (1997) observed a significant relation to the duration of SWS. In this study, statistically significant but small correlations between the *ssq* and SWS parameters were only observed for the PSM. Results in Tables 5 and 6 indicate that sleep efficiency during the second and the third quarters of the night seems to be an important sleep parameter increasing subjective perception of good sleep quality. Accordingly this negatively relates also to the number of awakenings and to the total wake time during these periods. Our previous studies showed significant but small correlations between these sleep parameters and the well-being and VAS test results (Rosipal et al., 2006). Higher loading values for well-being and VAS tests in comparison to *ssq* indicate that the first factor is strongly influenced by the variance of subjective sleep quality variables, which are not highly correlated with the considered sleep parameters. Therefore, it remains an open question if appropriate sleep parameters can be extracted from the used sleep models. Nevertheless, the study shows that *ssq* provides acceptable indexing of the subjective daytime evaluation of night sleep quality.

By testing the second and third factors against the individual physiological and neuropsychological variables they consist of it was observed that the factors show significantly higher or the same level of correlation with the sleep parameters. This was true for both the R&K and PSM sleep models. Therefore, these two factors were considered as good candidates for indexing objective daytime physiological and neuropsychological aspects of subjects. While both sleep models provided sleep parameters with similar level of correlations with *ssq* this was not true for physiological and neuropsychological factors. In terms of absolute correlation values and their variability the PSM was superior to the R&K model. Specific PSM sleep parameters like AUC and entropy revealed moderate correlations for almost all sleep stages. This was especially true when subjects younger than 40 years were considered. Recent studies by Gangwisch et al. (2006) and Knutson et al. (2009) showed

Table 6
Statistically significant ($\alpha = 0.01$) Spearman rank correlations (ρ) between the PSM sleep parameters and three variables representing subjective sleep quality (*ssq*), physiological test results (factor score 2) and neuropsychological test results (factor score 3). Statistically significant correlation values after Bonferroni correction are in bold. Abbreviations additional to Table 5 ent, entropy; auc, area under the curve. *Note*: the values of auc and relative auc (auc normalized by tib) were observed to be identical or differences small. For clarity of the table these two measures are not distinguished and the abbreviation auc is used.

Sleep stage	ssq subjective sleep quality		Factor 2 physiological		Factor 3 neuropsychological	
	Sleep par.	ρ	Sleep par.	ρ	Sleep par.	ρ
Wake	at	**0.33**	auc	0.23		
	auc	**0.32**	ent	0.23		
	atsp	**0.31**	q2/ent	0.19		
	q2/at	**0.27**	q3/at	0.19		
	q2/atsp	**0.27**	q3/rtst	0.19		
	q2/auc	**0.26**	q3/auc	0.18		
	q3/at	**0.25**	q4/auc	0.17		
	q3/atsp	**0.25**	at	0.17		
	q3/auc	**0.24**				
	q1/at	0.22				
S1	ent	0.21	q2/ent	**0.25**	q3/ent	0.16
	q1/ent	0.20	ent	**0.25**		
	q2/ent	0.20	q2/auc	0.23		
	q2/auc	0.18	q3/ent	0.20		
	auc	0.16	auc	0.20		
	q3/auc	0.16	q3/auc	0.17		
	q3/ent	0.15				
S2	q2/auc	**−0.29**	q4/auc	**−0.24**	auc	−0.19
	at	−0.23	auc	−0.22	q3/auc	−0.17
	q3/auc	−0.23	q3/auc	−0.17		
	q1/auc	−0.21	at	−0.16		
	q2/ent	−0.20				
	q3/at	−0.20				
	ent	−0.19				
S3, S4	ent	−0.21	q2/auc	−0.19	q3/auc	−0.17
	q2/ent	−0.20	q3/ent	−0.19	q3/ent	−0.16
	q3/ent	−0.20	q4/ent	−0.18	q4/auc	−0.15
	q2/auc	−0.17	ent	−0.17		
	q1/ent	−0.17	q2/ent	−0.17		
	q1/auc	−0.16	q2/at	−0.16		
	auc	−0.15	auc	−0.16		
			q2/rtst	−0.16		
REM			q2/ent	0.23		
			q3/rtst	0.18		
			rtst	0.17		
			q2/auc	0.17		
			ent	0.16		
GSP	eff	**−0.33**	q3/eff	−0.19		
	q2/eff	**−0.27**	eff	−0.16		
	tst	**−0.26**	q4/eff	−0.16		
	q3/eff	**−0.25**				
	q3/tst	**−0.23**				
	q2/tst	−0.23				
	q1/eff	−0.23				
	q1/tst	−0.20				
	q3/fw	0.18				
	q2/fw	0.15				

that short sleep duration (self-reported and wrist actigraphy based) was correlated with increased systolic and diastolic blood pressure leading to the risk for hypertension incidence. Interestingly, results in Tables 7 and 8 indicate additional sleep microstructure elements, which are significantly correlated with the physiological factor. Positive correlations of the factor with wake and S1 stage presence, number of sleep stage switches, or number of awakenings, and negative correlations with sleep efficiency and SWS presence are in accordance with the intuitive assumption that increased sleep fragmentation and less SWS may lead to increased blood pressure. The strongest correlations for these effects can be observed during the second half of the night (Tables 7 and 8). In contrast, no significant correlations were observed for sleep parameters computed during the first quarter of the night.

Negative correlations between SWS during the second half of the night and better performance in neuropsychological tests can be observed (see the last column of Tables 7 and 8). In normal sleep, SWS periods dominate in the first third of the night, but are often completely absent toward the end of the night and during early morning sleep (Dement & Vaughan, 1999). Therefore, we speculate that this increase of SWS being negatively correlated with attention, concentration, memory performance and motor activity elements of the morning measures may represent a form of sleep inertia. In contrast, good neuropsychological performance is correlated with increased amount of REM sleep (stronger correlations can be observed for the second and third quarters of the night). Karni et al. (1998) showed that REM sleep following a period of SWS is the most beneficial type of sleep for procedural memory enhancement. However, the design of the current study limits deeper interpretation of the observed results within the existing theories of sleep related motor skill improvement and memory consolidation (Siegel, 2001; Walker et al., 2002).

Table 7
Same as Table 6 but considering young subjects only (<40 years old).

Sleep stage	ssq subjective sleep quality		Factor 2 physiological		Factor 3 neuropsychological	
	Sleep par.	ρ	Sleep par.	ρ	Sleep par.	ρ
Wake	auc	0.31	ent	0.40		
	q3/auc	0.30	auc	0.37		
	q1/auc	0.28	q4/auc	0.37		
	at	0.27	q2/ent	0.37		
	q3/at	0.27	q3/ent	0.34		
	q3/atsp	0.27	q4/ent	0.33		
	atsp	0.27	q3/auc	0.31		
			q2/auc	0.31		
~~[5pt]~~ S1	q1/ent	0.27	auc	**0.44**	rtst	−0.33
	auc	0.27	ent	**0.43**	at	−0.31
			q4/auc	**0.42**	q3/ent	0.31
			q2/auc	0.41	q1/rtst	−0.30
			q2/ent	0.40	q1/at	−0.30
			q3/auc	0.39	q2/rtst	−0.29
					q2/at	−0.28
S2			q4/auc	**−0.42**	q2/auc	−0.31
			at	−0.36	q3/auc	−0.26
			q4/rtst	−0.35		
			auc	−0.28		
S3, S4			q2/auc	−0.37	q3/auc	**−0.48**
			q2/at	−0.33	auc	−0.38
			auc	−0.33	q3/rtst	−0.31
			q2/rtst	−0.33	q2/auc	−0.30
			q4/auc	−0.33	q4/auc	−0.30
			q2/ent	−0.32	q3/ent	−0.29
			ent	−0.31	q3/at	−0.29
			q4/ent	−0.30	rtst	−0.27
			rtst	−0.30		
			q3/auc	−0.29		
			at	−0.29		
REM	q4/at	0.31	q2/auc	0.40	q3/at	0.33
	q4/rtst	0.30	auc	0.38	q3/rtst	0.33
	at	0.27	q2/rtst	0.37	q4/at	0.33
			q2/at	0.36	at	0.32
			rtst	0.35	rtst	0.32
			q2/ent	0.35	q1/at	0.30
			at	0.34	q3/auc	0.30
			q3/rtst	0.33	q4/rtst	0.29
			q3/at	0.32	auc	0.28
			ent	0.32	q4/auc	0.27
			q3/auc	0.31		
			q4/at	0.31		
GSP	fw	0.29	fs	0.32		
	q3/eff	−0.28	q4/fw	0.29		
	q3/fw	0.27	fw	0.28		
	eff	−0.27	q3/fw	0.27		
			q3/eff	−0.26		
			q4/eff	−0.26		

Age related changes of sleep were reported in several studies (for example, Vitiello, 2006). Healthy aging is associated with decreased sleep duration, increased time and number of wake periods after sleep onset, decrease in SWS and others. While subjective perception of sleep quality does not seem to be age related, physiological and neuropsychological factors investigated in this study have shown strong age related effects in the group of subjects older than 40 years. This is in agreement with knowledge about age-related increase in variables like blood pressure, in memory or motor impairments characterized by longer response times, etc. Therefore, to avoid spurious correlations between sleep parameters and daytime measures, we compensated the effect by using a standard statistical technique of age detrending prior computing the correlations. However, it remains a subject of further studies if this is sufficient or different sleep models and daytime testing protocols directly compensating this effect need to be constructed. Other effects, for example the gender effect, were not studied in the current work.

The presented PSM allows moving away from the rigid structure of five sleep stages defined by the R&K rules and allows considering the finer structure of sleep microstates. Considering one of many possible grouping schemes of PSM sleep microstates resulted in the extraction of AUC and entropy related sleep parameters showing a higher level of correlation. Interestingly, the average number of the combined microstates was small indicating that there may exist sleep sub-structures reflecting important aspects of sleep related to the investigated subjective and objective indexes of night sleep quality.

It can be concluded that the presented concept of grouping a wider set of different sleep quality, physiological or neuropsychological performance measures into a smaller parsimonious set of usually not directly observed latent variables should be considered when searching for robust indexing of sleep quality. On the other side it seems that the standardized scoring of sleep into a set of discrete sleep stages may not be sufficient to reveal important sleep changes related to such indexes. For example, it may be true that

Table 8
Statistically significant ($\alpha = 0.01$) Spearman rank correlations (ρ) between the PSM sleep parameters computed from the combined sleep microstates and three variables representing subjective sleep quality (*ssq*), physiological test results (factor score 2) and neuropsychological test results (factor score 3). Statistically significant correlation values after Bonferroni correction are in bold. As in Table 7 young subjects were considered (<40 years old). Each value represents the average of the correlation values computed from 50 independent runs. Values in the brackets represent the average size of the combined sleep sub-state. Abbreviations are explained in Tables 5 and 6.

	ssq subjective sleep quality		Factor 2 physiological		Factor 3 neuropsychological	
	Sleep par.	ρ	Sleep par.	ρ	Sleep par.	ρ
Wake	auc	0.31 (2.5)	q4/ent	0.40 (5.3)	q3/ent	0.33 (2.9)
			auc	0.40 (5.4)		
			q4/auc	0.40 (5.2)		
			ent	0.37 (5.4)		
			q2/ent	0.37 (5.4)		
			q3/ent	0.35 (5.4)		
			q3/auc	0.35 (5.3)		
			q2/auc	0.33 (5.4)		
S1	q1/auc	0.31 (7.5)	ent	**0.44 (7.3)**	q3/ent	0.31 (5.2)
			auc	**0.43 (4.5)**		
			q2/ent	**0.43 (7.0)**		
			q4/auc	**0.42 (3.3)**		
			q4/ent	0.41 (4.0)		
			q2/auc	0.40 (8.7)		
			q3/ent	0.39 (4.7)		
			q3/auc	0.39 (2.8)		
S2			q4/auc	−0.40 (9.8)		
			q4/ent	−0.35 (7.2)		
S3, S4			q2/auc	−0.38 (4.8)	q3/auc	**−0.45 (3.6)**
			q4/auc	−0.37 (5.5)	auc	−0.40 (4.2)
			q2/ent	−0.35 (3.2)	q3/ent	−0.36 (4.3)
			auc	−0.34 (4.2)	q4/auc	−0.31 (4.5)
			ent	−0.33 (3.3)		
REM			q2/auc	0.40 (3.3)		
			auc	0.39 (5.1)		
			q2/ent	0.37 (3.9)		
			ent	0.35 (5.2)		
			q3/auc	0.34 (4.7)		
			q4/auc	0.33 (3.0)		

important information can be obtained from sleep models allowing continuously modeling transitions from one sleep stage into another. The PSM represents one of the possible ways how the standardized sleep staging can be extended and additional information incorporated; for example through sleep parameters like the AUC or entropy.

Although all presented correlations were statistically significant their absolute values were moderate or small. This is the case for all similar studies we are aware of, including studies referenced in this paper (Åkerstedt et al., 1994; Keklund & Åkerstedt, 1997; Saletu et al., 2005). Therefore, it cannot be expected that based on the observed relations reliable and precise prediction models between sleep parameters and subjective and objective indexes of sleep quality can be constructed. It remains an open question if considering the sleep process alone and without wider contextual information (for example, sleep deprivation, prior to sleep workload, or sleep environment factors) can lead to the extraction of more informative sleep parameters. On the other side, the current study has its own limitations, which are primarily given by the archival nature of the study. Therefore, it remains an open question if the considered measures of subjective sleep quality, daytime behavioral performance and physiological measures are sufficient to reliably reflect important changes of night sleep patterns, or a wider collection of tests and measures should be considered and tested.

Following the screening procedure of the SIESTA project the analyzed subjects were classified as healthy sleepers with normal sleep. The variance in the extracted sleep parameters and daytime measures can be expected to be reduced in comparison to the disturbed sleep population (sleep disorders resulting into sleep fragmentation, deprivation, etc.). We hypothesize that this lower variance may also lead to lower correlation values. Therefore, it is in the focus of our further studies to apply the presented methodology to patients with sleeping problems and to compare the obtained results.

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