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EDITORIAL

Rethinking Sleep Analysis

Comment on the AASM Manual for the Scoring of Sleep and Associated Events

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Visual sleep scoring is the obligatory reference for sleep analysis. An essential step in sleep scoring is sleep staging. This technique was first described in 1937 and later adapted 3 times: first, in 1957, after the detection of rapid eye movement (REM) sleep, when electrooculography (EOG) was added; second, in 1968, when sleep staging was standardized and electromyography (EMG) was added; and third, in 2007, to integrate accumulated knowledge from sleep science, adding arousals and respiratory, cardiac, and movement events. In spite of the dramatic changes that have taken place in recording and storing techniques, sleep staging has undergone surprisingly few changes. The argument of the present comment is that sleep staging was appropriate as long as sleep biosignals were recorded in the analog mode as curves on paper, whereas this staging may be insufficient for digitally recorded and stored sleep data. Limitations of sleep staging are critically discussed and alternative strategies of sleep analysis are emphasized.

Keywords: Sleep analysis, sleep staging, sleep scoring, visual analysis, automatic analysis

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The recently published American Academy of Sleep Medicine (AASM) manual for the scoring of sleep[1] defines rules for sleep stages and associated events, based on evidence reviews and the consensus of experts.[2] Methods of digital recording and analysis were reviewed in an accompanying paper[3] but did not receive a primacy for sleep analysis. Considering the enormous changes that have taken place with the spread of digital recording systems and the development of various algorithms to quantify sleep data, it is surprising to see that visual sleep staging still has the status of the gold standard for sleep analysis. In the following sections of this paper, the different limitations of sleep scoring by hand, as well as alternative strategies of computerized sleep analysis, will be discussed. Although many of these points have been debated earlier,[4-6] the implementation of the new AASM scoring manual deserves a rethinking of the process of scoring sleep stages. To better understand the pros and cons of sleep staging, one has to look from where it comes and how it developed as the primary technique of sleep analysis.

SLEEP STAGING, SOME HISTORICAL REMARKS

Only a few years after the invention of the electroencephalogram (EEG), it was Alfred L. Loomis who started a research project to study sleep in humans with the new EEG technology in his private laboratory at Tuxedo Park, New York. The personal and sociologic background of this research has been investigated in great detail in recent years.[7-9] Equipped with state-of-the-art amplifier technique and ink-writing recording systems, Loomis and coworkers were the first who performed whole-night EEG recordings of sleeping subjects and pioneered the essential electrophysiologic patterns of sleep in a series of ingenious papers. First they observed alpha activation after acoustic stimulation in sleep,[10] which contrasted with alpha blocking after stimulation in the wake state. Next, they described most of the essential EEG waveforms of sleep, namely sleep spindles, sawtooth waves, and random waves, later called K complexes or slow waves.[11] When examining long-term recordings of sleep EEG, they recognized that there were both slow developments and abrupt changes in the EEG pattern of sleep, and they concluded (p136) "...that the old idea of a continuous curve of sleep needs modification".[12] With a stroke of genius, they integrated the different EEG features of sleep into a set of 5 levels or states of sleep (A to E), spanning the continuum from wakefulness to deep sleep.[12,13] The time course of sleep with the transitions between states was depicted graphically as a 2-dimensional plot with time on the abscissa and the sleep stages on the ordinate. Although they clearly defined the time axis in physical terms, Loomis' group made efforts to validate the order of the 5 sleep states against measures of depth of sleep. They showed that the degree of arousability decreased from A to E, whereas movements were most prominent in states A and B, and a change in state was frequently connected with a body movement.[12,13]

The newly developed scoring system had to be reworked when REM sleep was recognized as a different state of sleep

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in 1953. In a first step, Dement and Kleitman[14] used a revised scoring system to differentiate EEG patterns of sleep and distinguished among 4 EEG stages, which they called stages 1 to 4. When they could show that the incidence of the newly detected REMs in sleep coincided with stage 1, only sparing stage 1 at the onset of sleep, the new classification of EEG states of sleep was quickly adopted by others. The new system became standard for staging human sleep when the scoring rules were standardized by a committee of experts a few years later.[15]

THE DIMENSIONALITY OF SLEEP

As long as sleep was conceived as a unitary process, although separated into different levels or states, the order of states was assumed to be linear, proceeding from wakefulness to deep sleep.[12] A new situation arose when REM sleep was recognized as a different state of sleep with specific features and regulatory mechanisms.[16,17] Although the sequence of non-REM (NREM) sleep stages 1 to 4 (R&K classification[15]) or N1 to N3 (AASM classification[1]) fulfills the criteria of an ordinal scale, with a linear order of stages but variable intervals, the addition of REM sleep resulted in a more complex metric of sleep states. An adverse consequence for sleep analysis was that the new scoring system has only nominal scale quality, with a nonlinear order of stages and variable intervals. For this reason, it is only by convention whether REM sleep is represented either on the top[14] or on the bottom[18] of the sleep profile. The low metric of sleep stages limits mathematic operations to addition or subtraction, and, as a consequence, the most common statistical descriptors of sleep stages are simple measures, such as latencies and amounts (minutes or percentages) of stages, or derived measures, such as sleep efficiency. For this reason, more ambitious approaches to model sleep in a mathematic way bypass sleep staging and make use of variables with higher scale quality, such as power of EEG frequency bands.[19] However, this does not exclude the possibility of also modeling sleep on the basis of sleep stages, as Feinberg[20] and Gaillard[21] showed in early sleep-modeling studies. The latter author foresaw (p89): “Leaving aside byzantine discussions about what sleep stages are and are not, future research may point to another kind of digitalization of sleep. In that case, the same methodology will be applicable and will make it possible to transform the all-or-nothing variables into continuous functions of sleep.”[21] Here, again, the concept of sleep as either a continuous or discontinuous function appears, which pulls itself like a red thread through electrophysiologic sleep research.

Alternatives for Sleep Analysis

Although the conventional manner is to represent the time course of sleep as a sequence of states or stages along the time axis, alternatives have been conceived. Steriade and McCarley[22] used a 3-dimensional indicator space to illustrate the definition of waking, EEG-synchronized sleep, and REM sleep. This concept was developed further by Hobson et al,[23] who suggested a 3-dimensional state-space AIM model to represent the states wake, NREM sleep, and REM sleep along the 3 axes: *activation* (A; from high to low), *input source* (I; from internal to external), and a *modulation* (M; from aminergic to cholinergic). The trajectory that connects the 3 states in the state space was modeled earlier by Massaquoi and McCarley.[24]

Another alternative to represent the changes of cerebral activity during sleep was suggested by Koella,[25] who developed the concept of *local vigilance* to describe the actual readiness of individualized systems, such as neural, motor, vegetative, or other systems. In sleep, the “vigilance profile, i.e., the level of a variety of local vigilances, changes fundamentally again with the transition from NREM to REM sleep.” (p1429) [25] Although the subject is in deep NREM sleep, the local vigilance of electrocortical systems is low and the local vigilance of motor systems is high. As a consequence, NREM parasomnias are typically associated with motor acts but without conscious awareness. The reverse is true for REM sleep, with a high vigilance of electrocortical systems and low vigilance of the motor systems. Koella concluded (p1433): “These pre-programmed variations in local vigilance of the many behavioural systems are so obvious that one may seriously consider using the vigilance profile as the foundation for a badly needed, new *functional principle of sleep staging*.”[25]

THE SUBDIVISION OF NREM SLEEP

Another critical point in sleep staging is the definition and demarcation of the NREM sleep stages. Although human visual analyzers are extremely skilled in pattern recognition and in the flexible adaptation of a set of rules that define sleep stages, they are poor in handling slow changes, as the changes typically occur in the background EEG, e.g., changes in the number, duration, and amplitude of slow waves of NREM sleep. Such changes in the EEG can only be transformed into scoring rules by the application of quite arbitrary threshold criteria, as they were used to differentiate between sleep stages 3 and 4 in the Rechtschaffen and Kales manual.[15] For just this reason, sleep stages 3 and 4 were combined into a single stage (N3) in the new AASM scoring manual.[1] The decision for only 1 sleep stage, characterized by EEG slow waves, greatly reduces the tedious and time-consuming work load for the human scorer to count the occurrence and amplitudes of delta waves, whereas, at the same time, the cost of the decision is an increase in intrastate variability. Multidimensional statistical analysis suggests that sleep stages are inhomogeneous and can be subdivided into smaller, more homogeneous units.[26] The fact that sleep stages are nonhomogeneous units is also known from experimental studies. Brandenberger et al,[27] for example, who analyzed autonomic and hormone data during sleep, presented evidence for 2 substates of stage 2 sleep, a quiet one that precedes the transition into slow-wave sleep and an active one that precedes REM sleep. Other approaches to decompose the heterogeneity of sleep stages were suggested earlier by Molinari and Foulkes,[28] who differentiated between tonic and phasic segments of NREM and REM sleep. Later Terzano et al[29,30] introduced the concept of cyclic alternating patterns (CAP), a NREM pattern of transient electrocortical activity, which is distinct from background activity. The nonhomogeneity of the stages of normal sleep indicates that sleep staging is in no way exhaustive and much information is lost. Part of this information is nowadays summarized under the broad label *microstructure* of sleep, which contains patterns, arousals, CAP, and any other event with a latency or duration shorter than the half-minute epoch of sleep staging.[31,32]

Alternatives for Sleep Analysis

Kemp[33] has presented the outline of a computer-based digital sleep analysis that differentiates between wake, REM sleep, and NREM sleep, whereby the latter is seen as a continuous-scale function. The representation of NREM sleep as a continuous function has also been suggested by others.[34,35] To ensure accuracy, the proposed sleep analyzer uses a minimum time resolution of 1 second. All features, extracted from EEG and non-EEG signals (e.g., cardiac, respiratory, movement, or other signals), are arranged in the same format, thus also allowing a detailed analysis of the interaction between the different signals. The high time resolution and the continuous scale for NREM sleep avoid the quite artificial breakdown of the feature space into separate classes of micro and macro events, which are a consequence of visual sleep staging.

Another concept for analyzing digital sleep data has been proposed by Agarwal and Gotman.[36] In a first step, the polygraphic record is segmented into pattern-specific segments of variable-length epochs followed by a second step of self-organization of the segments into variable groups of homogeneous clusters. Different algorithms for sleep analysis by the segmentation technique have been developed.[37,38]

SCORING SLEEP BY EPOCHS OF FIXED DURATION

Sleep scoring is traditionally based on 30-second segments of sleep records, called epochs. The segmentation with a fixed epoch length of 30 seconds goes back to Loomis et al,[39] who used a "paper cutting brain potential recorder" with a roll of paper, which was cut by a knife each 30 seconds, corresponding to 30 cm of paper.[39] Later, Dement and Kleitman[14] retained scoring of a "fairly long stretch of record," since shorter classifications, made every few seconds (p676), "would give the misleading impression of excessively frequent alternation between stages."[14] The decision was justified mainly with the changing pattern during a spindle stage and with the waxing and waning of delta waves. An epoch length of 30 or 20 seconds, depending on paper speed, was also recommended by the R&K manual. Although longer (1-minute) epochs have been used by some groups,[40] shorter epochs have been used only for research purposes. The AASM manual[1] also recommends sleep scoring in 30-second sequential epochs. This epoch duration is economic for hand scoring and quite accurately reflects the time course and macrostructure of normal sleep, without the danger of too many stage shifts. In spite of these advantages, half-minute epochs are less suited to depict short-lived events, such as arousals,[41] movements, or critical respiratory events, which are common in patients with a sleep disorder. As a result, sleep staging is generally less reliable if sleep is fragmented, as occurs in most patients with sleep disturbances.[42-44]

Alternatives for Analysis

As an alternative to using epochs of a fixed duration, adaptive segmentation has been proposed for EEG[45-47] and sleep analysis to identify and cluster quasi-stationary segments of variable duration.[37,48-50] Another method to analyze and represent short-lived patterns or changes in the background signal is the wavelet transform,[51,52] which differs from the Fourier transform by the way in which the information of the signal is localized in the time-frequency plane. In contrast to the Fourier transform, information of the time of occurrence and phase is retained in wavelet analysis.

FROM SINGLE-CHANNEL TO MULTICHANNEL SLEEP RECORDINGS

Another critical point for sleep analysis by hand is the rapid expansion of data assessment in sleep recording. Although early scoring was restricted to a very limited number of recording channels (EEG, EOG, and EMG), the recording of a variety of additional channels (respiratory, cardiac, additional EEG and EMG traces, and others) has become standard practice and, therefore, has been defined with recording techniques and standard parameter extraction in the new AASM scoring manual.[1] The additional signal analysis according to arousal rules, cardiac rules, movement rules, and respiratory rules imposes a heavy load on the human visual analyzer.

Alternatives for Analysis

There is no obvious reason why the time-consuming task of analyzing the increasing mass of physiologic variables in sleep recordings should not be delegated in toto to automatic analysis. The human part in the man-machine interface of sleep analysis could be restricted essentially to 3 major tasks, (1) definition and development of algorithms; (2) surveillance of the analysis process, including artifact decontamination; and (3) quality control of sleep analysis.

The results of the automatic analysis could be filled into a state plane, which is defined by the states waking, NREM sleep, and REM sleep, as discussed above. Such a systematic representation of physiologic signals, analyzed with a high time resolution, would also allow a systematic study of the interaction of signal changes in 2 or more channels, which is not feasible on the background of the traditional sleep staging. Finally, the questionable separation of events into 2 different classes, representing the so-called macrostructure and microstructure of sleep, could be avoided. Although, at present, sleep-stage–bound measures are summarized as the macrostructure of sleep, all short-lived events are summarized as microstructure of sleep. This separation is quite artificial and results mainly from the fact that there is a large number of short-lived events, which are not represented in sleep stages.

SLEEP STAGING—VISUAL OR COMPUTERIZED?

Although sleep staging was developed as a technique for visual sleep analysis, over the years, many attempts of computerized sleep staging have been made.[3] In most cases, algorithms have been constructed in such a way that the results match the outcome from visual scoring with the R&K rules as closely as possible. There is a large amount of literature on the agreement rates between both approaches.[3,44,53] Problems that hinder a straightforward and generally accepted solution have been mainly related to peculiarities of the R&K rules, artifact recognition, and individual differences in electrophysiologic sleep signs. The latter point was already strongly emphasized by Loomis et al.[12] Although the human analyzer is quite good in adapting to such modifications, this is more difficult for computerized scoring systems. If a computerized analysis of rule-based sleep stages is intended for any reason, the comparison of visual and automated scoring should differ from past strategies in some major points.

Alternatives for Analysis

Comparisons of the performance of visual and computerized sleep stage scoring has historically been a 1-way street, since the results of visual scoring have been taken as reference to compare the agreement between visual and automated scoring. As a consequence, a systematic analysis of mismatched epochs is missing in the literature. Such an analysis of discrepancies between both data sets could be used as a basis for a revision of computer algorithms and of the visual scoring rules as well. This would help to define areas in which the computer is superior, e.g., in quantifying EEG background activity; areas in which both analyzers may be equal in performance, e.g., pattern recognition; and areas in which the human analyzer is more proficient, e.g., in the recognition of relationships between events in different recording channels or in artifact detection.

CONCLUSION

Sleep scoring and sleep profiling have deeply molded our understanding of the physiologic sleep process. However, since the method is restricted to a limited set of EEG, EMG, and EOG features, other features and biosignals are treated separately. A typical consequence of such a procedure is the separation between the so-called macrostructure and microstructure of sleep.

Because sleep scoring is based on the analysis of epochs with a fixed time duration, the method is not flexible enough to recognize short-lasting events or to analyze the temporal relationship between such events in different channels. Thus, sleep staging reduces the multilayer and time-varying physiologic processes of sleep into a rule-based set of a few sleep stages, which are conventionally presented in the form of a 2-dimensional sleep profile. Although sleep scoring was appropriate and sufficient for analog sleep recordings with only a few recorded signals, multichannel recording of digital data during sleep has opened new possibilities that are only poorly reflected in the traditional sleep stages. Visual sleep staging should no longer be taken as the blueprint of the sleep structure, which is then accomplished by a multitude of additional visually or automatically analyzed parameters. Future sleep analysis should aim at integrating different levels of data extraction, based on a set of algorithms to identify the changing features in biologic functions during sleep. Acceptance of automatic sleep analysis in the sleep science community will be dragging as long as visual sleep staging is accepted as gold standard and sleep stages are seen as biologic units rather than useful descriptors of the sleep process needed for manual scoring.

Points for a Research Agenda

1. Future sleep analysis will be based on a fully digitalized data-acquisition platform. This allows a highly reliable and cost-effective data analysis. Although systems and software packages for the acquisition and analysis of sleep data are already available, it will be the task of the sleep science community to set the rules and guidelines for the further development of such systems.
2. The digital data structure allows the quantification of the occurrence and characteristics of all EEG and non-EEG signals of sleep. Studies have shown that specific features of the electrophysiologic signals of sleep correlate with plastic processes, associated with memory formation, or aging. This underlines the usefulness and validity of direct sleep-signal analysis for clinical and research purposes.
3. The signal features can be back projected to the sleep-wake cycle and to the REM-NREM cycles to depict and analyze their temporal distribution and regulation.
4. It has to be explored whether and if, affirmative, in which way electrophysiologic signals can be combined into higher order units or substates of sleep.
5. Sleep staging should be no longer the gold standard for sleep analysis.

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