

Spotlight on Sleep Stage Classification Based on EEG

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Abstract: The recommendations for identifying sleep stages based on the interpretation of electrophysiological signals (electroencephalography [EEG], electro-oculography [EOG], and electromyography [EMG]), derived from the Rechtschaffen and Kales manual, were published in 2007 at the initiative of the American Academy of Sleep Medicine, and regularly updated over years. They offer an important tool to assess objective markers in different types of sleep/wake subjective complaints. With the aims and advantages of simplicity, reproducibility and standardization of practices in research and, most of all, in sleep medicine, they have overall changed little in the way they describe sleep. However, our knowledge on sleep/wake physiology and sleep disorders has evolved since then. High-density electroencephalography and intracranial electroencephalography studies have highlighted local regulation of sleep mechanisms, with spatio-temporal heterogeneity in vigilance states. Progress in the understanding of sleep disorders has allowed the identification of electrophysiological biomarkers better correlated with clinical symptoms and outcomes than standard sleep parameters. Finally, the huge development of sleep medicine, with a demand for explorations far exceeding the supply, has led to the development of alternative studies, which can be carried out at home, based on a smaller number of electrophysiological signals and on their automatic analysis. In this perspective article, we aim to examine how our description of sleep has been constructed, has evolved, and may still be reshaped in the light of advances in knowledge of sleep physiology and the development of technical recording and analysis tools. After presenting the strengths and limitations of the classification of sleep stages, we propose to challenge the “EEG-EOG-EMG” paradigm by discussing the physiological signals required for sleep stages identification, provide an overview of new tools and automatic analysis methods and propose avenues for the development of new approaches to describe and understand sleep/wake states.

Keywords: scoring, electrophysiology, visual, automatic, recommendation, artificial intelligence

Introduction: From Physiology to Sleep Stages, a Historical Perspective

Since the first electroencephalography (EEG) recordings in humans by Hans Berger in 1929,¹ the way physiologists and sleep physicians identify wake-sleep related EEG changes has largely evolved. Until 1968, sleep stages were identified using rules that varied according to scientific teams and to breakthroughs in sleep physiology such as the description of rapid-eye-movement (REM) sleep by Dement and Kleitman in 1957 and Jouvet in 1959.^{2,3} In 1968, a group of sleep researchers led by Allan Rechtschaffen and Anthony Kales was created in order to establish a consensus about the way to classify sleep stages based on electrophysiology recordings. At that time, sleep studies were mostly physiological studies on healthy and young subjects aiming to describe and understand sleep mechanisms. The Rechtschaffen and Kales (R&K) manual of sleep staging⁴ was adopted by the worldwide sleep scientific community and then by the sleep clinicians when medical sleep units started to develop in the late 1960s and 1970s⁵ with exponential increase during the past two decades. With the application of R&K rules in the clinical field and the need to identify pathological conditions, as well as the digital revolution of EEG recordings in the 1990s, voices rose from the sleep medical community to amend these rules.⁶ The American Academy of Sleep Medicine (AASM) organized a taskforce to adapt some criteria of original

R&K manual and define pathological sleep events. Sleep staging recommendations were published in 2007⁷ and repeatedly updated since then,⁸ notably taking into account criticisms from the international sleep specialists community pointing out some limitations in the changes of several criteria, such as arousals, the number of EEG channels or the use of these criteria in specific populations^{9–13}. In the meantime, the understanding of sleep physiology and sleep disorders has evolved; although somewhat shaped by these rules, this knowledge has also shown their limitations with regard to the dynamical properties of sleep whose features evolve on time scales shorter than 30-second epochs, and which are modulated by various factors such as sleep cycles, homeostatic pressure, and age. Furthermore, determining pathological thresholds and correlating objective biomarkers provided by sleep staging with the subjective symptoms associated with sleep disorders remains a challenge, although it is critical for clinical practice. Thus, even though AASM recommendations remain the gold standard for sleep staging worldwide, the scientific community has started to develop alternative methodology to describe sleep, based on EEG or non-EEG sensors, using artificial intelligence, and, for some, departing from classical sleep stages. In this perspective paper, we propose to provide a historical, physiological and technical overview of how the sleep stage classification was thought and built. We discuss the potential changes that may occur as knowledge evolves, also considering factors limiting such changes. We first present the strengths and limitations of the current procedure to score vigilance states. Next, we discuss the physiological signals required for sleep stages identification and provide an overview of new tools and automatic analysis methods. Then, we propose avenues for the development of new approaches to describe and understand sleep/wake states. Our goal is to put into perspective the historical background generating our current sleep staging rules with the recent developments in physiological and methodological research, in order to provide keys to open new research avenues which will aim to better capture the complexity of sleep/wake physiology and identify biomarkers for sleep disorders.

Strengths and Weaknesses of Sleep Stage Classification

Current Rules for Sleep Stage Classification

According to the AASM recommendations,^{7,8} three types of electrophysiological signals are mandatory to properly identify wakefulness, non-REM (NREM) sleep, REM sleep and arousals. The recording of these signals requires at least three scalp EEG electrodes, two electrooculography (EOG) electrodes located from either side of the eyes and two chin electromyography (EMG) electrodes placed above and below the chin with a third back-up electrode placed below the chin. Scalp EEG electrodes are located in frontal (F3 and/or F4), central (C3 and/or C4) and occipital (O1 and/or O2) areas according to the 10–20 international system,^{14,15} and referenced to an electrode located on the contralateral mastoid. An alternative montage using bipolar channels of the median line (Fz-Cz and Cz-Oz) in association with a referential channel C4-M1 is allowed. EOG is also recorded with a referential montage, with both EOG electrodes being referenced to the same mastoid electrode. Only chin EMG channel is a bipolar channel between the two studied chin EMG electrodes. Electrophysiological recordings are segmented in 30s epochs, which sequentially scroll during sleep staging process. The sleep specialist scores each epoch of recording belonging to a period called time in bed, defined as the duration between lights-off and lights-on. A general principle of sleep staging recommendations is that an epoch is considered to pertain to a specific vigilance state if more than 50% (15s) of that epoch has the electrophysiological features of this vigilance state. An epoch is staged as wakefulness if 50% of this epoch consists of alpha activity (8–13 Hz) in the occipital region or if some movements artefacts specific to wakefulness are observed, such as blinking, eye movements associated with reading activity or rapid eye movements associated with high muscle tone. An epoch is staged N1 stage if at least 50% of this epoch consists of low voltage mixed frequency activity comprised between 4 and 7 Hz, replacing alpha activity in patients generating alpha rhythm. This EEG activity may be associated with slow eye movements and/or vertex sharp transients which are physiological EEG features occurring during N1 and N2 stages. In people not generating alpha rhythm, the first epoch of N1 stage is attributed to the first epoch containing i) at least 50% of EEG frequency in the theta band between 4 and 7 Hz with background EEG activity slowing-down at least 1 Hz below wakefulness EEG background activity, or ii) slow eye movements, or iii) sharp wave transients. Usually following N1 stage, the first epoch of N2 stage is attributed to the first epoch containing K complex or sleep spindles in the first half of the epoch. Continuity of N2 stage is allowed as

far as there is no arousal nor criteria for N3 or REM sleep. An epoch is scored as N3 stage if slow waves are present during more than 20% of the epoch (6s). Slow waves are defined as 0.5 to 2 Hz frequency waves with a peak-to-peak amplitude of 75 μ V measured on the frontal derivation in reference to the contralateral mastoid. Finally, an epoch is staged as stage R (REM sleep) if more than 50% of this epoch contains all the following: i) low voltage mixed frequency EEG activity without sleep spindle nor K complex; ii) minimal chin EMG tone, including during rapid eye movements; iii) rapid eye movement at any moment of the epoch. Continuity within a same sleep stage or transitions between two distinct stages are defined by various rules not detailed in this paragraph, and which consider in particular the effect of arousals or major body movements.

Sleep Stage Classification, A Common Language

This sleep stage classification, which is a human construct based on neurophysiological discoveries dating back to the first part of the last century, is used by all sleep physicians and researchers in the world since more than 50 years and has been regularly updated, most recently in 2023.^{4,7,16} Its dissemination and widespread use in both sleep medicine and research fields, as well as its status as a “gold standard” have, however, exceeded its initial objectives. The reasons for its success are manyfold: First, the (relative) easy access to EEG, EOG and EMG with inexpensive recording devices, as compared to imaging for example, and low technical complexity even if the placement of electrodes remains time consuming; second, the precision

of guidelines for PSG recording allowing standardization of practices all over the world; third, the (also relative) simplicity of the scoring process, with easy-to-refer-to rules, without the need for complex analysis systems as long as signals can be visualized and the stage/events can be marked with a user-friendly software. Fourth, its clinical usefulness for the diagnosis of sleep disorders such as sleep-related breathing disorders, sleep-related motor disorders, parasomnia and hypersomnia, keeping in mind that standard polysomnography parameters remain disappointing for the most frequent sleep disorder, ie, insomnia, which somewhat dampens its clinical relevance;^{17,18} Fifth, the dissemination as recommendations by the main sleep society, the AASM, and the integration of sleep scoring in the training curriculum of young sleep physicians and researchers.^{19,20} Last but not least, the former R&K manual and the current AASM recommendations have the great advantage of providing the bases for a common language. Sleep researchers and sleep physicians use the same rules to stage sleep, which allows to build comprehensive bridges between basic research in humans and research on sleep disorders. In basic research on rodents, there is still no consensus on the definition of sleep stages, which can be a source of error especially for transitional states but is also an avenue for future researches.²¹ In human sleep staging, referring to common rules allows a satisfactory interrater reliability in sleep description.^{22,23} In a recent meta-analysis, Lee et al studied all the articles assessing interrater reliability of adult sleep staging since the R&K manual publication in 1968.²⁴ The authors eventually included eleven studies and distinguished between Cohen’s k for overall sleep stages (seven studies) and Cohen’s k for each sleep stage (four studies). Considering Cohen’s k for overall sleep stages, they found a Cohen’s k of 0.76 [0.71–0.81], showing a substantial agreement between scorers. A European project, the SIESTA database, specifically studied interrater reliability for overall sleep stages when using R&K rules compared to AASM rules.²⁵ The authors found a higher interrater reliability with the AASM versus R&K rules (Cohen’s k of 0.76 and 0.68, respectively), interpreted as the result of additional EEG channels in AASM recommendations. However, interrater reliability is lower when considering separately each sleep stage. In their meta-analysis, Lee et al found a substantial agreement for stage W and R, moderate agreement for N2 and N3 and only fair agreement for N1 stage.²⁴ N1 stage is not a stable sleep stage. It is highly influenced by transitions between wakefulness and sleep onset and between sleep stages when arousals occur. In their interrater reliability program, Rosenberg and van Hout also found the poorest interrater reliability in stage N1.²² They observed that scorers often failed staging epochs during the transition between wakefulness and N1 and between N1 and N2. They also reported that scorers had difficulty discriminating between N2 and N3. These issues highlight the limitations of human scoring, which do not completely remove the subjectivity of interpretation and, by simplifying a complex phenomenon, do not capture the many facets of sleep/wake states.

Limitations of Sleep Stage Classification to Describe the Complexity of Physiology

Beyond methodological limitations due to the epoch-based scoring, difficulties in scoring sleep transitions may also result from sleep physiology itself. Sleep staging is based on long distance montages of scalp EEG recordings, which provide a very global picture of brain activity and are unable to record EEG activity from deep structures.^{26,27} Studies investigating sleep physiology with intracerebral EEG recordings have brought valuable information on sleep/wake transitions and spatial heterogeneity of sleep within different brain areas. In particular, stereo-electro-encephalography (SEEG) allows to record EEG activity of deep brain regions. SEEG recordings are exclusively performed in patients with drug-resistant focal epilepsy as part of pre-surgical work-up when the epileptogenic zone cannot be identified using non-invasive techniques. Studies of human sleep physiology with SEEG recordings have highlighted that transitions between wakefulness and sleep are progressive and asynchronous within the brain. Sarasso et al showed that, at sleep onset, sleep spindles were observed in the hippocampus up to 30 minutes before neocortical regions, which was recently confirmed and extended to other sleep stage transitions.^{28–30} Such a spatio-temporal dissociation was also demonstrated between the thalamus and the neocortex.³¹ Beyond sleep onset, SEEG studies have shown that regional differences in EEG sleep/wake patterns persisted during whole-night sleep and were also observed during the sleep-to-wake transition.^{32,33} In addition, specific sleep oscillation also exhibit regional specificities and disparities, as reported for NREM sleep spindles in the neocortex^{34,35} and in the thalamus,³⁶ as well as for REM sleep sawtooth waves³⁷ and NREM sleep slow waves,³⁸ similarly to what was previously published in rodents.³⁹ Interestingly, local slow waves have also been detected in awake animals, leading to the concept of “local sleep”,⁴⁰ a mechanism hypothesized as causing attentional lapses in humans.⁴¹ Besides intracranial EEG recording, restricted to a sample of patients with drug-resistant focal epilepsy, non-invasive recordings with a higher spatial resolution than the AASM-recommended EEG montage may help to capture the spatial complexity of sleep in subjects without epilepsy. These types of recording generally require a higher number of sensors (ie, high-density (hd)-EEG or magnetoencephalography), sometimes coupled with MRI in order to increase spatial resolution, as well as a specific expertise in EEG signal processing. Regional and electrophysiological changes occurring during sleep-onset were studied using techniques such as source localization⁴² or combined EEG-MEG recordings,⁴³ with results showing regional changes during the transition between wakefulness and sleep. Spatial analysis may also help clinicians to better interpret PSG recording and analyze sleep disorders. Regional differences in EEG activity between the first as compared to the second night of PSG recording in healthy subjects were shown using hd-EEG, suggesting that the first-night effect also impacts regional brain activity during sleep.⁴⁴ Studies investigating microsleeps during an active task,⁴⁵ or focusing on sleep inertia,⁴⁶ insomnia,⁴⁷ and disorders of arousal⁴⁴ also benefitted from such regional analysis based on non-invasive recordings, which brings keys for a better understanding of the pathophysiology of sleep disorders. All these works highlight the heterogeneity of sleep/wake states between brain regions as well as the great permeability between sleep/wake states (Figure 1).

In addition to the spatial limitation of scalp EEG, current sleep stage classification rules also show a limitation in detecting and quantifying the complexity of sleep microstructure and dynamics. Markers of sleep instability extracted from polysomnography reports based on AASM recommendations mainly consist in the number of sleep stage changes and the arousal index. An arousal is defined as an abrupt change of EEG frequency including alpha, theta and/or frequencies higher than 16Hz (excluding spindles) lasting at last three seconds and occurring after a ten seconds duration of stable sleep.⁴⁸ However, arousals identified with AASM rules do not entirely capture sleep instability. In 1985, Terzano et al described a new EEG marker of physiological NREM instability, the “cyclic alternating pattern” (CAP).⁴⁹ During CAP sequences, EEG activity repeatedly shifts between activity phases (phase A) and background activity (phase B). Phases A are divided in three sub-types: type A1, represented by synchronous EEG activity such as delta bursts, K-complex sequences, vertex sharp transients, polyphasic bursts with <20% of EEG desynchrony; type A2, defined as a mixture of slow and fast rhythms with less than 50% of EEG desynchrony; and type A3, in which EEG activity contains more than 50% of rapid low-voltage rhythms (see Parrino et al, 2012 for review).⁵⁰ To note, 96% of A3 and 62% of A2 sub-types correspond to arousals according to the AASM classification.⁵⁰ The increase or decrease in CAP sequences as well as the subtypes of A phases were then studied in sleep or neurological disorders, bringing new insights

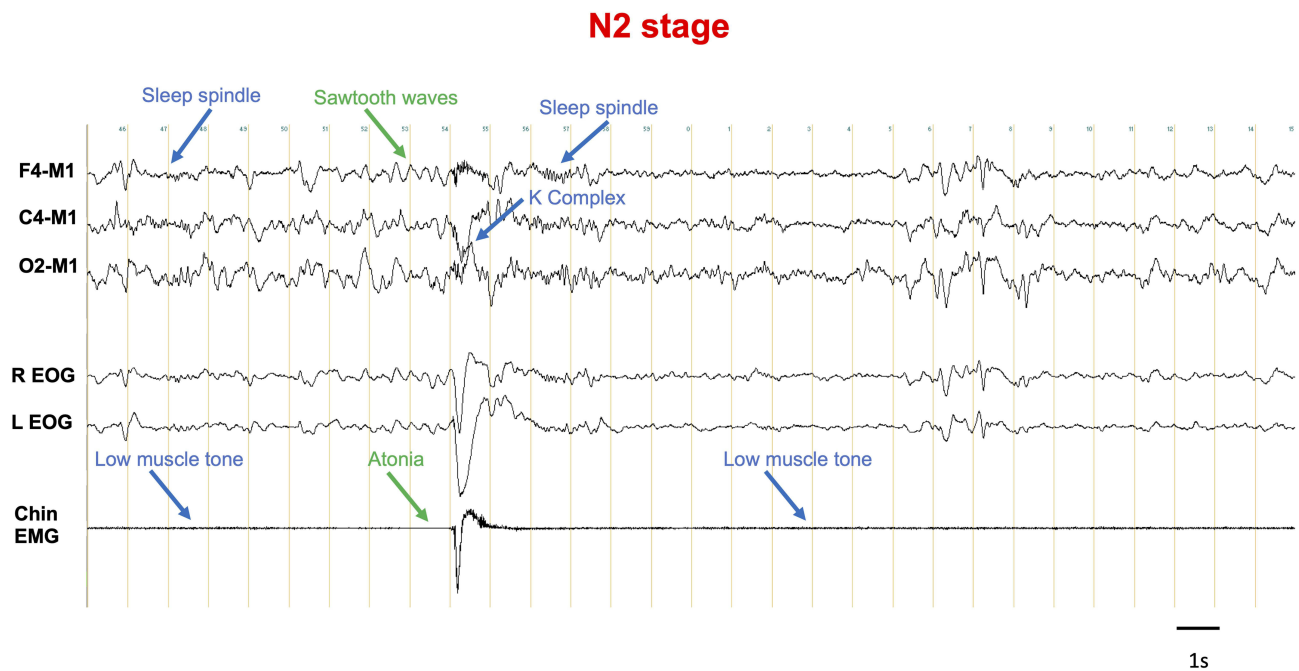


Figure 1 Intra-Epoch Heterogeneity In Sleep Stages. In this N2 epoch, one can see both N2 features (in blue: low muscle tone, K complex, sleep spindles) and R features (in green: sawtooth waves and transient atonia). This example highlights that the 30s scale does not capture the complexity of the dynamics of vigilance states. **Abbreviations:** R, right; L, left; EOG, electro-oculogram; EMG, electromyogram.

on sleep phenotyping in these disorders.^{51–53} Nevertheless, the use of this tool to describe NREM has remained in the research domain and is not integrated in the AASM recommendations.

Signal Perspective: Which Signal(s) are Needed to Score Sleep? Categorization of Vigilance States Using EEG, EOG and EMG

Fluctuations between states of vigilance are characterized by physiological changes in most body functions,⁵⁴ but the categorization and identification of wake, NREM and REM sleep traditionally relies on only three parameters: EEG, EOG and EMG. Despite its wide use, this classification, which may prove cumbersome and reductive, is increasingly being questioned under the influence of different clinical and research trends. In sleep medicine, the better understanding of certain sleep disorders, such as insomnia, central disorders of hypersomnolence, or sleep apnea, is leading to the search for biomarkers that are better correlated with clinical symptoms, prognosis and whose diagnostic performance is higher.^{55–58} On the research side, the development of increasingly complex signal analysis tools allows to extract more information from the available data, and the progress in the understanding of the spatiotemporal dynamics of vigilance states highlights the limits of current scoring, as detailed above.^{59–64} Most of these markers rely on EEG advanced analyses, but some of them focus on others signals such as heart rate variability, oximetry or respiratory signals.^{58,65}

Therefore, the issue of moving away from the “EEG/EOG/EMG” paradigm arises, and raises different questions: 1) do we need all three parameters (EEG/EOG/EMG) to stage sleep, whereas exploring brain activity (EEG), which reflects the processes regulating states of vigilance and controlling most physiological parameters, might be sufficient? 2) if EEG only allows to classify sleep stages, how many and which channels are needed? 3) do we really need the EEG or could we consider using other physiological signals, easier to access and/or prone to provide complementary information about sleep?

Categorization of Vigilance States Using EEG Only

It is well known among neurophysiologists that the information contained in the EEG far exceeds that used in the scoring rules. However, the exploitation of this information depends on the scorer (and their experience, as well as the limitations

of the human eye and brain, eg, for high frequency analysis) and on the recording specificities (settings including the montage, sampling rate and filters). The scoring rules have been designed for a particular montage with a low number of electrodes (F4-M1, C4-M1, O2-M1), and the preferential topography as well as the specific amplitude of certain features, such as the 75 μV peak-to-peak amplitude for slow waves, critically depend on this montage (Figure 2).⁸ In practice, several EEG montages are used and, if in the end the scoring result is not significantly affected by the AASM EEG montage (recommended versus acceptable Fz-Cz, Cz-Oz, C4-M1),⁶⁶ a higher number of available electrodes is associated with a better inter-scorer agreement and might result in changes in sleep staging and arousal detection.^{12,25,67}

The question whether sleep staging might rely on EEG only, without EOG or EMG, is not only important from a physiological and technical point of view (does the EEG signal contain enough information to differentiate vigilance states and are we able to extract and interpret this information?) but also from a practical perspective, in the context of long-term in-hospital VideoEEG monitoring, as well as for the development of wearable home devices. Information extracted from EEG signal may also bring critical information on sleep structure, as demonstrated by the use of time-frequency analysis implemented in most sleep analysis software, which is solely based on EEG information and allows to identify the changes of EEG dynamics during a whole-night, as a tridimensional function of EEG frequency, EEG power and time (Figure 3).

The example of epileptology is striking. Epileptologists have a great deal of expertise in EEG, and it was shown that scoring based on 27-electrode videoEEG had a 95% agreement with scoring based on PSG, even in patients with an abnormal EEG.⁶⁸ Interestingly, Cohen's kappa was very high for both arousals (0.89) and REM sleep (0.96), despite the absence of EOG and EMG. To note, the EEG signal does not only correspond to brain activity as it is contaminated by other electric signals, physiological or not. Artefacts (such as eye movements and muscle activity) are useful clues, and are more likely to be recorded when the number of EEG channels is high.

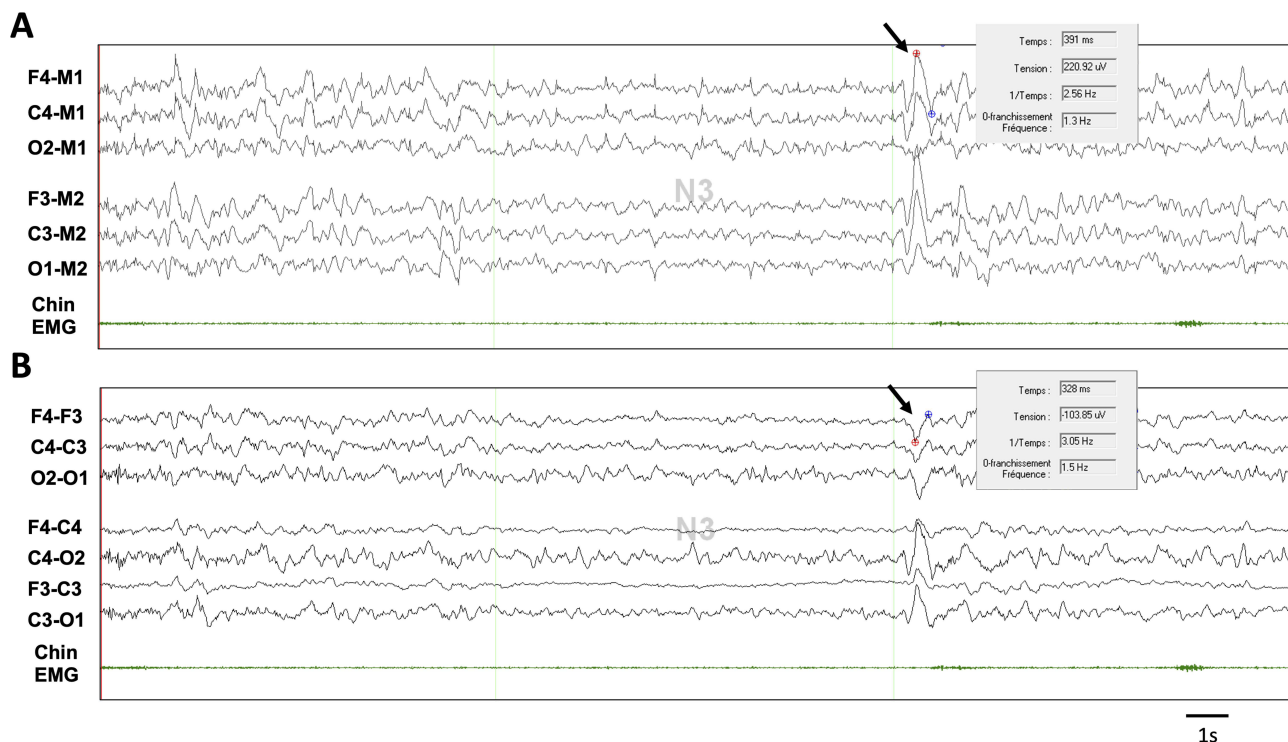


Figure 2 Peak-to-peak amplitude of slow waves according to different EEG montages. This N3 epoch is shown with the AASM recommended referential montage (A) and in a bipolar montage (B) with transverse (up) and longitudinal (down) channels. Both panels are visualized with an amplitude of 10 $\mu\text{V}/\text{mm}$ for EEG channels. The peak-to-peak amplitude of the same slow wave is measured on two different channels (black arrow). The amplitude is higher using the AASM recommended montage on the frontal channel (220.92 μV in (A) compared to the transverse montage (-103.85 μV in (B) with a negative value due to the inverse polarity). Also note that in (B) the maximal amplitude of this slow wave is not in observed frontal channels.

Abbreviations: M1, left mastoid, M2, right mastoid.

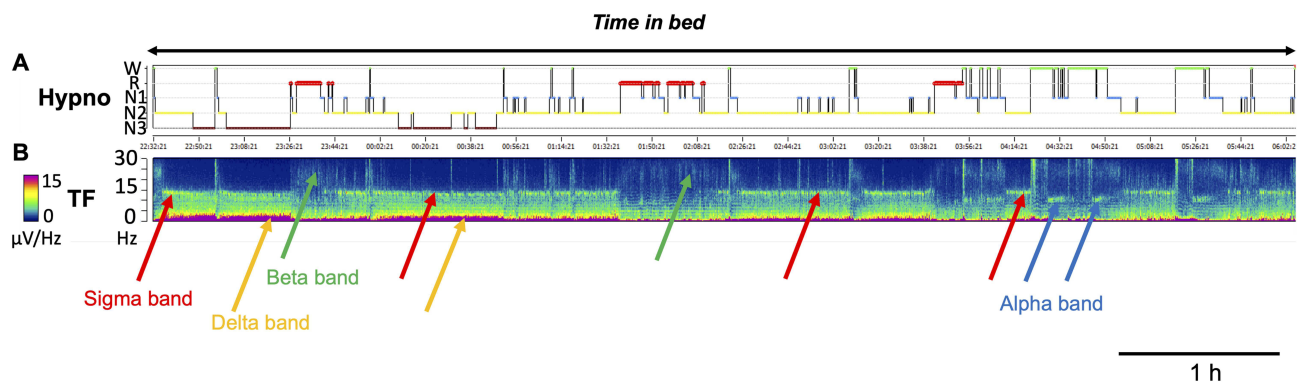


Figure 3 EEG Time-Frequency Analysis During Sleep Recording. Hypnogram obtained from AASM recommended sleep staging in (A and B) shows the corresponding spectrogram trend of EEG frequency measured on C4-M1 channel derived from a fast Fourier transform analysis. Color-bar indicates the power of EEG frequency ($\mu\text{V}/\text{Hz}$ with the lowest power in dark blue and the highest power in red), the y-axis indicates the EEG frequency (from 0 to 30 Hz) and the x-axis indicates time. The EEG signatures of NREM include an increase in the delta band below 2 Hz (Orange arrows, compatible with slow waves) and in the sigma band around 15 Hz (red arrows, compatible with spindle activity). The power of delta activity decreases across the night along with the decrease of homeostatic pressure. An increase in beta activity is observed in REM sleep (green arrows). At the end of the recording, note the EEG activity in the alpha band around 10 Hz (blue arrows, compatible with quiet wakefulness eyes closed). **Abbreviations:** Hypno, hypnogram; TF, time-frequency analysis; M1, left mastoid.

For cost/effectiveness obvious reasons, there have been many efforts to develop automatic sleep scoring (feature-based shallow learning or deep neural networks) using EEG only, based on multi- or single-channel analysis.⁶⁹ Overall, the performance of single-channel EEG-based automatic scoring, as assessed by agreement with visual scoring based on EEG/EOG/EMG by a human expert, is slightly lower than that of multi-channel EEG or multi-signals approaches especially for REM sleep.^{70,71} However, validation studies conducted in healthy adults have shown good performances with Cohen's kappa ~ 0.8 on average.^{72–77} Several works have also demonstrated fair agreement with visual scoring in patients with sleep disorders.^{78–80} Results seem to be influenced by the choice of the EEG channel (better performances for frontal leads), but innovative methods of accessing the EEG, such as Ear-EEG, have been proposed.^{80–83} These research studies show that the loss of information due to the reduction in the number of sensors can be compensated for by a better exploitation of the data included in the available signals. This may allow for the development of simpler, portable, ambulatory sleep exploration devices.^{84–86} This also suggests that advanced analysis of other physiological signals could be possibly used as an approach to identify vigilance states.

Categorization of Vigilance States Using Other Electrophysiological Signals Than EEG

Is the EEG the gold standard for sleep staging? While the investigation of sleep with EEG, possibly with additional channels to cover more brain regions, may seem the most suitable way to understand sleep, one should keep in mind that the information provided by the scalp EEG is limited to the superficial dorsolateral cortex and ignore regions (such as the hippocampus or the occipital cortex) where sleep is not only very different but also asynchronous.^{28,31,87,88} In addition, many other physiological functions and parameters fluctuate according to states of alertness, which go far beyond the brain.⁵⁴ These limitations, which may explain the discrepancy between subjective correlates of sleep or symptoms and prognosis of sleep disorders on the one hand, and objective sleep parameters on the other hand, temper the supremacy of the EEG and leave room for other approaches. Thus, the huge development of initiatives to develop automatic sleep scoring over the last past 20 years has led to various methods regarding both the type of recorded signal and the method to analyze it. Among them, one can cite EOG-based sleep scoring, which achieved performances close to those based on EEG for 4 to 6-stage classes (W, R and, depending on the study, 2 to 4 stages of NREM sleep) sleep staging, probably because the EOG signal contains not only information from eye movements but also from the EEG.^{89,90} Recently, good results for sleep staging (4 or 5 classes) have been reported with actigraphy, in addition with heart rate variability and acceleration features⁹¹ or peripheral arterial tone, keeping in mind the low performances of actigraphy for discriminating light NREM sleep when used alone.⁹² Some authors have proposed the use of respiratory movements, alone or coupled with movement signal to perform macro-sleep stage (Wake/NREM/REM) classification^{93,94} and even sleep mandibular movements, first aimed to detect apnea, have shown fair performance for sleep staging (4 classes).⁹⁵ The analysis of

sleep sounds (related to breathing, movements, etc.) recorded with non-contact microphones⁹⁶ of movements (body movements, respiration amplitude and frequency) with non-contact biomotion sensors⁹⁷ was also reported to enable macro-sleep stage (2 to 4 classes) scoring. Such approaches may allow to monitor sleep without contact sensors and are intended to be less disturbing for sleep.

All these technologies are attractive because of their simplicity and their performances seem convincing.^{89–97} In addition, they offer an alternative to standard laboratory sleep studies whose availability is limited considering the huge prevalence of sleep disorders. There are, however, some limitations that should temper the enthusiasm for their use. First, most of them only provide a discrimination between wake and sleep states or between wake, NREM and REM sleep, and for some of them enable the diagnosis of sleep disorders such as obstructive sleep apnea, but do not allow a precise classification of sleep stages and even less an analysis of sleep microstructure. Second, most of these tools were tested in specific databases, and the performance may drop if they were used in other datasets. Third, one of the objectives of their development is the use in clinical practice, which means that they must be validated in various sleep disorders and populations including children, whereas most of them have been studied in healthy adult individuals or in obstructive sleep apnea only. Finally, sleep physicians know that in practice, even if recordings are at best monitored in hospital by technicians, it is not uncommon to lose one of the signals during part of the night. The availability of other sensors makes it possible to compensate for these technical incidents. Thus, the use of a single signal without back-up may limit the relevance in practice.

Prospects in Sleep Staging Thinking Outside the R&K and AASM Rules

“What is simple is false and what is not is useless.” wrote Paul Valéry.⁹⁸ The simplification of vigilance states dynamics by AASM rules that try to segment a continuum physiological process, necessarily faces many limitations when it comes to describing pathological conditions. Regardless of the approach (human or automatic scoring), or the type of physiological signals used, constraining the description of sleep to this rigid framework is associated with obvious pitfalls. Thus, it might be relevant to challenge the standard “30 s sleep stage” scoring scheme which originated from physiological observations, but has turned into a top-down injunction. The tremendous development of signal recording and analysis techniques, including the speed of analysis of large amount of data, could be an opportunity to return to a data-driven approach.⁹⁹ This may enable to better quantify sleep or wake instability, as well as transitional states which may be the very states (“fragility zones”) interesting in sleep and neurological disorders. This would remove from scoring algorithms the absurdity of having to replicate the human ‘gold standard’, which is necessarily imperfect, and which itself deviates from the purposely simplified rules, to adapt to physiological variability.

What Would Be the Perfect Scoring System?

Considering what could be an alternative to standard sleep stages requires thinking about what can be expected from it, in order to shape its development. The first objective would be to describe physiology, in its complexity and multiple dimensions, and to capture the multiple regulatory processes, in particular from a research perspective. This might require combining information from time scales other than 30s and potentially from different global/local spatial scales. The second objective would be to provide quantifiable metrics correlated to subjective or behavioral variables, but also, for application to sleep medicine, to clinical symptoms, and, in the best case, to prognosis (complications, etc.). Third, this system should be quick to disseminate, open access, and simple to implement and use. Probably, in the perspective of personalized medicine, this scoring system would have to adapt to various populations, taking into account the diversity (age, gender, ethnicity, etc.).^{100–103} Finally, at a time when work on Big Data is exploding and public health needs are exponential, it is likely that this system would rely mainly on artificial intelligence, provided that a critical human eye remains capable of detecting possible errors or inconsistencies. The number and heterogeneity of these requirements suggest that the development of such a system for describing and quantifying vigilance states might be utopic and that hierarchical choices will have to be made. A consensual reflection between researchers, doctors, engineers and developers appears in any case crucial.

Conclusion

Polysomnography remains a cornerstone of sleep research and medicine, even if alternative initiatives are proliferating, either using other signals to match the classical sleep stages, or using other dimensions than sleep stages to describe vigilance states. These new approaches are based on recent advances in our knowledge of sleep regulation mechanisms and on progress in data processing and analysis. They contribute in turn to our understanding of sleep physiology and pathophysiology. However, to date, the vast majority of these new approaches are still being tested/validated against polysomnography which remains the definite gold standard. Is classical polysomnography really an obligatory passage point for describing and studying sleep?¹⁰⁴ In any case, it seems likely that the use of electrophysiological signals will remain a core part of sleep assessment. One of the specificities of the sleep research and medicine lies in its technical aspects, in the search for tangible objective elements to oppose, compare or correlate to the great phenomenological variability linked to sleep. Thus, it is difficult to predict how the many new available technical tools will be integrated into the medical and research landscape, and whether and how, beyond informing us about other dimensions of sleep, they may one day bridge the gap between validation studies and large-scale dissemination. The strong interest of our community in these issues, whatever the underlying motivations, nevertheless augurs well for considerable changes in the coming decades.

Abbreviations

AASM, American Academy of Sleep Medicine; CAP, cyclic alternating pattern; EEG, electroencephalography; EOG, electrooculography; EMG, electromyography; SEEG, stereo- electroencephalography; NREM sleep, non rapid-eye-movement sleep; R&K, Rechtschaffen and Kales; REM sleep, rapid-eye-movement sleep.

Disclosure

The authors report no financial or non-financial conflicts of interest in this work.

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