

Sleep Architecture and Its Relationship to Insomnia

Milton K. Erman, M.D.

The methods used to obtain and depict sleep data shape our understanding of sleep as a phenomenon. The standard criteria for describing sleep were developed in the late 1960s. These criteria, which were established on the basis of the polysomnographic equipment available at that time, called for the division of sleep into stages according to depth; the visual depiction of these stages led to the now widely accepted concept of "sleep architecture." Although the sleep architecture model remains useful, the technology that provided the model's framework for understanding sleep has been superseded by computer-assisted systems for recording and analyzing sleep that may allow us to acquire data on sleep that were unobtainable with older equipment. Future gathering and depiction of sleep data, regardless of the recording and assessment methods used, should minimize disruption of sleep during study, allow for computerized analysis of sleep parameters, and describe the data from the perspective of the effect that sleep and the problems surrounding it have on daytime functioning.

(J Clin Psychiatry 2001;62[suppl 10]:9-17)

A review of sleep architecture generates questions that are perhaps almost as much related to philosophy as they are to physiology. What is sleep architecture, and why should we be concerned with it? *Sleep architecture* is a term that has become widely accepted, perhaps without sufficient concern with regard to the validity of the concept. In preparation for this article, I reviewed the sleep literature in an effort to try to delineate the first use of the term, without success. Use of a term such as *sleep architecture* implies the capacity to accurately describe the shape or boundaries of a phenomenon such as sleep, as well as to infer or describe the structural elements that comprise it and hold it together. This further implies an assumption that data used to generate these hypotheses reflect an accurate "scientific" understanding of the components which make up sleep.

THE EVOLUTION OF THE UNDERSTANDING OF SLEEP

Historical Explanations

How has sleep been perceived in the past? From a historical perspective, sleep has been both mysterious and feared. Night, historically, was a dangerous and unsafe period. Night and sleep have both had strong associations

with and ties to death. A statue excavated from the ruins of a Greek temple in Sicily provides what can be considered an early effort at understanding sleep and its circadian phase relationships. The statue is a representation of the goddess of the night, Hypnos, suckling her twin sons, Somnos, sleep, and Thanatos, death. Whether we were able to awaken from sleep each night, to be brought back from the brink of death, was perceived to lie in the hands of the gods.

All religions help individuals to understand and deal with elements of our world that otherwise may seem incomprehensible. Such a framework of belief may help us to deal with complex issues that confront us on a daily basis in our lives, including birth, death, illness, loss, and sacrifice. In a life so uncertain and so little controlled by man that it was felt that the soul left the body each time we sneezed, it is not surprising that sleep engendered tremendous fear and wonder. The uncertainties and mysteries of sleep—fear of death in the night, concern with regard to the location and control of the soul as we slept—led to prayer at bedtime that one would be able to arise in the morning and prayers of thanks in the morning for being revived, restored by sleep, and even capable of discerning the difference between day and night.

Fascination with dreams and their meanings dates to greatest antiquity. The dream, with its confusing and powerful imagery, was perceived to have meaning long before Freud began his efforts at dream interpretation. Typically, it was believed that dreams held within them information that could be used to predict the future. Fragments of papyrus from 2000 B.C.E. deal with dream interpretation. In the Bible, Joseph gains his freedom in Egypt, and later great political power, through his capacity to use dream interpretation to successfully predict the future.

From the University of California San Diego School of Medicine and Pacific Sleep Medicine, La Jolla, Calif.

Presented at the symposium "New Developments for Treating Sleep Disorders," which was held March 24, 2000, in Chicago, Ill., and supported by an unrestricted educational grant from Wyeth-Ayerst Laboratories.

Reprint requests to: Milton K. Erman, M.D., Pacific Sleep Medicine, 9834 Genesee, Ste. 328, La Jolla, CA 92037.

Freud saw the dream as powerful in another context, allowing us to gain insight into elements of mental function that are hidden from us in any conscious context. His belief that “the interpretation of dreams is the royal road to a knowledge of the unconscious activities of the mind” was a determining factor in the role that review and interpretation of dream content has played in psychoanalysis.^{1(p608)} Freud’s fascination with dreams, and his belief that the dream allowed understanding of mental pathologies, helped stimulate later interest in the study of sleep, and especially rapid eye movement (REM) sleep, as a possible probe into the understanding of mental illness of various types.

Early Scientific Explanations

Science also makes efforts to provide explanations to increase our understanding of the mysteries of the universe. As with religion, scientific concepts of sleep have changed over the ages. We no longer talk of “humors” as did Hippocrates, or suggest, as did Alcamon, a contemporary of Pythagoras, that sleep resulted from the retreat of blood and warmth into inner regions of the body. What of the “scientific” study of sleep? Science, historically, is concerned with description and categorization of phenomena. From this perspective, formal study of sleep could not have begun until the 20th century, with recognition of the existence of “brain waves,” electroencephalographic (EEG) activity, first recorded by Berger in 1928.² The existence of such activity, and the recognition of differences in EEG between sleep and wake, meant that sleep could be measured and recorded without awakening the sleeping subject. This was a necessary step in the process of categorization of sleep states and comparison of brain activity between sleep and wakefulness. Use of the sleep EEG as a tool in describing the activity of the brain in sleep was advanced by the work of Loomis and colleagues in the 1930s.³ Their work refuted the notion of sleep as a static state of brain rest, demonstrating that brain activity as measured by EEG changed over the course of the night.

Dr. Nathaniel Kleitman may be considered the first modern sleep researcher. Beginning in the 1920s with research on the impact of sleep deprivation and culminating in the publication of his landmark work, *Sleep and Wakefulness*, in 1939,⁴ Kleitman’s original research included many observations that contributed dramatically to our current understanding of sleep physiology. Professor Kleitman engaged himself in many areas of research that remain of great interest today, in particular his exploration of circadian control of sleep tendencies. The discovery of REM sleep by Aserinsky and Kleitman in 1953,⁵ with recognition of the existence of cyclic changes in sleep over the course of the night, may well be considered the physiologic foundation upon which all modern sleep research is based.

THE CURRENT STANDARD FOR DESCRIBING SLEEP ARCHITECTURE: THE R AND K CRITERIA

What does the term *sleep architecture* mean and how is it used? A synonym for *architecture* is *structural design*. In considering the architectural design of a building, we use descriptive terminology. We believe that we can describe the building, define its size and shape, and, using our knowledge about the materials with which it is constructed, understand how it works, how the parts and sections relate and interact. Of course, if the data we have are erroneous—if materials listed on the plans have been substituted or omitted—the assumptions we make about the appearance, strength, or integrity of the structure may be inaccurate.

Background

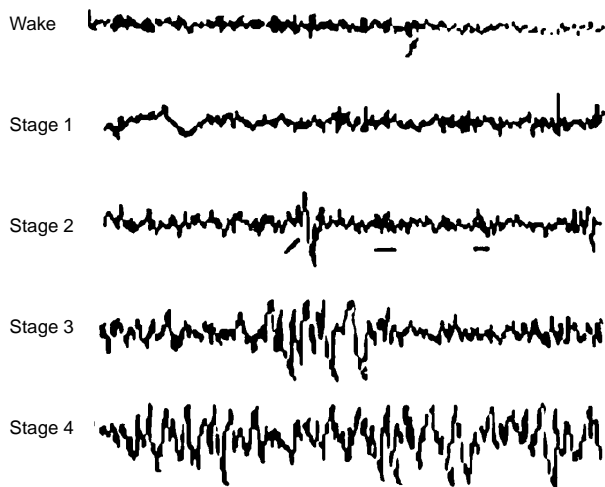
The term *sleep architecture* thus refers to a system that allows us to describe sleep and its boundaries (wake and drowsiness) and the structural elements that give it shape and substance. Extending this analogy from the architecture of buildings and their structural components, the sleep structural element that is most relevant is the concept of sleep stages. The system of describing and staging sleep that has had essentially universal acceptance uses sleep criteria published in a work edited by Rechtschaffen and Kales, published in 1968.⁶ This system, which uses REM and non-REM (NREM) sleep stages to define sleep architecture, was derived from an earlier system proposed by Dement and Kleitman.⁷ These systems, developed after the description of REM sleep, made obsolete the older Loomis system that classified sleep in stages A through E, but could not categorize REM sleep.

The Rechtschaffen and Kales criteria, or “R and K criteria,” as they are commonly described, were an advance in the description of sleep, using the best data available in 1968.⁶ A summary of the basic elements of this system is appropriate. The R and K criteria were based on a standardized approach to polysomnographic (sleep recording) techniques, using recording equipment that was state of the art in 1968. At that time and for many years after these criteria were established, all sleep recordings were recorded on paper, using EEG machines or more specialized sleep recording equipment. A specified paper speed of 10 mm/sec was designated, which yielded 30 seconds of recording data on a standard page of EEG paper. This led to a “standard” 30-second recording epoch, within which sleep was defined as being present if wave forms characteristic of sleep were present during at least 15 seconds of the epoch.

Components

Core elements of the R and K system include the division of all sleep into REM and NREM sleep, as well as the separation of NREM sleep into stages 1 through 4. That 2 very distinct states of sleep, REM and NREM, exist is very

Figure 1. Electroencephalographic Activity During Wake and the 4 Stages of Non-Rapid Eye Movement Sleep



well supported by the totality of sleep research and all that we understand about sleep physiology. Myriad distinctions between these 2 states can be identified in functions such as the presence or absence of rapid eye movements, middle ear muscle activity, muscle tone, and erectile function. EEG activity, cardiac and respiratory rate and rhythm, and temperature regulation also differ dramatically between REM and NREM sleep. These types of differences support the notion that these are very different states and, as had been suggested, may well differ from each other as much as they are different from the other major state of consciousness, wakefulness.

Validity

Does the division of NREM into stages 1 through 4 have as much clinical and research validation? Not at all. We see the range of EEG activity in wake and NREM sleep presented in Figure 1. Although there are dramatic differences between the EEG patterns displayed, NREM sleep is a continuous state. We are not able to define a clear transition between stage 2 and stage 3 sleep, for example, as we can between REM and NREM. Rather, we may observe “deep stage 2 sleep,” reflecting deepening of sleep, with an increase in amplitude and greater slowing of EEG, but not reaching the arbitrary threshold for entry into stage 3 (20% of the epoch comprised by sleep in a delta range) required by the R and K criteria.

However, the division of NREM sleep into stages 1 through 4, with greater “depth of sleep” associated with the higher numbers, is both clearly rational and reflective of the physiologic variability associated with these states. Stage 1, with a transition from wakefulness into drowsiness and entry into sleep, is clearly a state from which arousal occurs readily. Arousal may be generated by any

type of stimulus—auditory, visual, tactile, etc. With transition into stage 2 and into delta sleep, arousal thresholds are higher, no matter what the type of stimulus. Thus, the notion that as sleep progresses from stage 1 through stage 4 it becomes “deeper” is both understandable and supportable. The notion that this deeper sleep—sleep from which it is harder to be awakened—is automatically the most restorative sleep is not a necessary conclusion, however.

Another way to assess the validity of such a taxonomy is to see how well it defines states of health and disease. From such a perspective, it can be argued that the R and K criteria are actually quite effective. If we look at the sleep of patients with insomnia complaints, we find specific abnormalities in sleep architecture that correspond to many of these patients’ subjective complaints. The objective sleep latency of individuals with insomnia is indeed prolonged compared with the sleep latency of those without insomnia, whether we use criteria of latency to first epoch of stage 1, to 3 epochs of stage 1 or any epoch of stage 2, or more rigorous criteria requiring 5 or 10 minutes of continuous, persistent sleep. Insomniac patients report that their sleep is “light” and report frequent awakenings. In most objective studies of the sleep of individuals with insomnia, we see evidence of these processes in terms of increased amounts of “light” stage 1 sleep, with more frequent and persistent transitions to wakefulness and more time spent awake during the night.

LIMITATIONS OF THE CURRENT STANDARD FOR UNDERSTANDING SLEEP ARCHITECTURE

The question must be raised as to whether the principles of sleep architecture established by the R and K criteria confirm the specific complaints of insomnia patients. These complaints include prolonged sleep latency and dramatically shortened total sleep times, including the not-infrequent perception of some patients that they have slept little, or not at all, over the course of the night of study. The answer to this question is a resounding no. Despite the observations noted above about the concordance of subjective complaints and objective findings, insomnia patients are generally inaccurate in their estimates of sleep latency and total sleep time, dramatically overestimating their latency to sleep onset and underestimating their total sleep time. In the most extreme representation of these tendencies,⁸ patients may report that they obtain little or no sleep at all over the course of the night. Despite the report of sleep amounts of as little as an hour or 2, these patients are not sleepy in the daytime and generally are unable to nap, even when given the opportunity. When studied polysomnographically, the amount of sleep these patients obtain, although not normal, is substantially greater than the amount they believe they have obtained.

Does such a discrepancy suggest that a system such as that defined within the R and K criteria is invalid? Not at

all. Abnormalities of sleep continuity—transient “micro-arousals,” the intrusion of alpha wave activity, and other elements reflecting lightening of sleep without shifts to full wakefulness—may be present in many types of sleep disorders, including sleep apnea, periodic limb movements in sleep, and sleep-related bruxism. The disruption of sleep continuity associated with these disorders may not grossly affect the overall sleep architecture or measures such as sleep latency or sleep efficiency, but may well explain the subjective complaints of fatigue and lack of restorative benefit of sleep that patients with these conditions report. Unfortunately, the R and K system has no way of assessing the presence of these types of arousals or reflecting their impact in scoring.

As we consider the variance in EEG associated with the stages shown in Figure 1, other questions related to the structure of the R and K system become apparent. The first has to do with the conceptualization of stage 1, the lightest stage of sleep and the normal transitional phase between wakefulness and sleep. Does entry into stage 1 clearly signify sleep onset? If not, what is it? Entry into stage 1 sleep is defined by the presence within a 30-second period of a period of greater than 15 seconds during which elements of stage 1 appear. These elements include reductions in or the disappearance of posterior waking alpha wave activity and reductions in slow-rolling eye movements characteristic of drowsiness, which precedes entry into sleep, and the appearance of slowing in the EEG generally represented by theta wave activity. In general, sleep onset is considered to have occurred when 3 consecutive 30-second epochs of stage 1 sleep are seen or when the appearance of any epoch of deeper sleep (stages 2, 3, and 4 of NREM or any REM sleep) is seen. Although this may seem a precise and scientific definition, it is actually more arbitrary than may be obvious. For example, does the presence of 3 consecutive epochs of sleep, each of which contains an arousal and 14 seconds of wakefulness, reflect the same situation as a transition within 90 seconds from stage 1 sleep to deep stage 2 or stage 3?

If entry into stage 1 does not clearly signal sleep onset, does it clearly define a state of consciousness different from drowsy wakefulness? We know that many individuals report a capacity to be aware of and remember auditory stimuli and wake-like mentation present in stage 1 sleep, prior to entry into stage 2. In most studies, the measured interval between lights out and the appearance of stage 2 sleep corresponds closely to subjective sleep latency. An argument can certainly thus be made that stage 2 corresponds more precisely with true entry into sleep, and in many research studies, this criterion (or a criterion such as 10 consecutive minutes of sleep without an awakening) is used to define sleep onset. Considering such an approach may help us to better understand and deal with reports that we hear from patients that, despite the fact that our graphs say that they were asleep, they know that they were awake, dozing or drifting in and out of sleep.

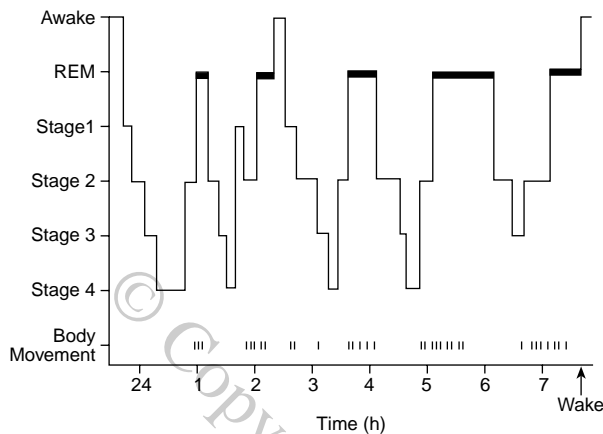
Questions can also be raised about the significance of EEG waveforms that are used to define the presence of stage 2 sleep. Naturally occurring spindles and K complexes seen in stage 2 sleep help to mark entry into (and the continuance of) a state of sleep that is “deeper” (i.e., more resistant to arousing stimuli) than stage 1 sleep. However, these sleep elements may also be generated by other causes. Benzodiazepine sedative and hypnotic agents generate large numbers of sleep spindles; K complexes may be generated by sleep apnea arousals or in association with disorders in which spontaneous arousals may appear, with repetitive disruption of sleep. Is sleep that has such elements of pharmacologically generated spindles or intrinsically or extrinsically generated K complexes deeper and more restorative than naturally occurring stage 1 sleep?

HOW CAN SLEEP DATA BE DEPICTED THOROUGHLY AND ACCURATELY?

When a system developed to describe any phenomenon is used as widely and for as long a period of time as has the R and K system, it becomes a part of “institutional memory” and is accorded a status that verges on the religious. Of course, there is nothing sacred about such definitions, and as data are generated that define limitations of such a system, the system is modified or discarded. The R and K criteria have proven their worth over the more than 30 years since their publication, but some real limitations are associated with the technology that was available at the time of their production. Computerized sleep recording and analysis systems now widely available can generate similar displays of 30-second “pages” or epochs, but also provide the capacity to examine sleep over varying periods, from an “epoch length” of as short as 10 or 15 seconds to one of as long as 15 minutes, an hour, or the entire night. These varied intervals provide perspective on cyclic aspects of sleep physiology and pathology that may not be evident using the classic 30-second epoch length. These systems also provide the capacity for automated analysis of EEG activity, which may allow greater objectivity in the assessment of EEG waveform characteristics, for example, than is available even by the visual assessment of a trained scorer.

In considering how we characterize what we record in sleep, we must be concerned about making an assumption that what we record is of relevance simply because we have the capacity to record it. We are certainly strongly committed to concepts of the importance of REM and NREM, and we have a great deal of information about the importance of these elements in terms of such phenomena as emotional regulation, memory storage, and immune function. However, we should also remind ourselves that just because we can record these signals from the surface of the brain, we cannot be sure that these elements are of

Figure 2. Typical Progression of Sleep Stages Over the Course of the Night^a



^aAbbreviation: REM = rapid eye movement.

critical importance in understanding brain function in sleep. For example, should we be concerned that benzodiazepines can suppress delta sleep, when patients tell us that the sleep they obtain with the use of these drugs is deep and restorative? What of the observation that the monoamine oxidase inhibitors can suppress REM sleep completely for protracted periods of time, during which treatment patients show return to normal function with regard to severe symptoms of depression?

Sleep architecture is of relevance in the assessment and management of insomnia. Although patients with insomnia complaints are not able to accurately estimate sleep latency or time spent asleep, when studied in the sleep laboratory they show abnormalities in sleep architecture that usually correspond to their subjective complaints. Those whose sleep data show protracted objective sleep latencies and low sleep efficiencies usually describe problems entering sleep and large amounts of time spent awake over the course of the night.⁹

Strong statements about improvements in sleep architecture associated with hypnotic treatment can be made. When insomnia patients are treated, those who receive hypnotic medications, compared with those who receive placebo, report greater improvements in sleep quality, reductions in sleep latency, and increases in total sleep time.^{10,11} These same improvements are all also seen in objective sleep measures obtained in polysomnographic studies. Reductions in numbers of arousals and improvements in sleep continuity seen with use of hypnotics are reflected in reports of improved sleep quality no matter what the source of sleep disruption, including disorders such as sleep apnea and chronic obstructive lung disease.^{12,13}

A failure of the sleep architecture model in the assessment of insomnia is its incapacity to account for residual effects of hypnotic medications after awakening. Excel-

lent data have been obtained from numerous studies^{14,15} showing that medications with long, intermediate, and even short half-lives can lead to impaired performance in the daytime following nighttime use. However, the tendency for such impairment is not reflected in analyses of sleep architecture over the course of the night, and the persistent sedative effect would even lead to better results with regard to sleep duration, total sleep time, and sleep efficiency. As with virtually all medications, we must consider the next-day effects with these medications and the fact that more is not necessarily better. As their doses are raised, probabilities of side effects—particularly impairment of alertness, memory, and motor performance—will increase. Half-lives clearly play a major role in the probability that these events will occur and will also determine for how long impairment may persist.

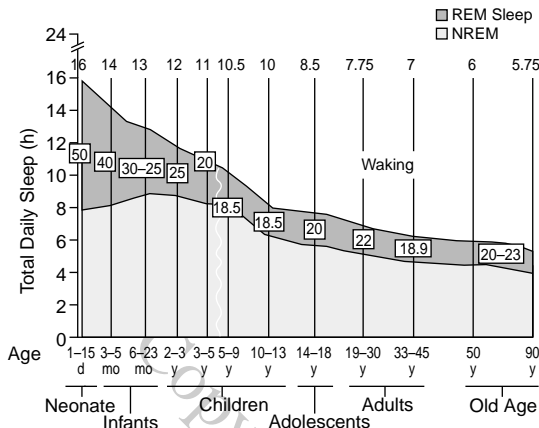
Specific Methods of Depicting Sleep Data

The data generated by scoring of sleep can be represented in various manners. A sleep hypnogram, as seen in Figure 2, provides a 2-dimensional visual representation of the progression of sleep stages over the course of the night. The hypnogram may give us a clue to at least one of the origins of the term *sleep architecture*, since what we see is very reminiscent of the outline of the buildings of a city skyline. A problem with the sleep hypnogram is that it may lead colleagues who are not sleep specialists to infer that the position of sleep stages on the hypnogram reflects their position as stages of deeper or lighter sleep. This may lead to confusion, since if the assumption is made that deeper stages of sleep—stages 3 and 4—are seen at the bottom of the hypnogram, how do they compare to REM sleep, seen at the top of the hypnogram?

In addition to portraying variations in sleep physiology over the night, graphs can represent the progression of sleep over the life cycle (Figure 3). These data from Roffwarg and colleagues¹⁶ give a measure of changes in total sleep time and sleep stage preponderance over the life cycle. This is another representation, perhaps, of sleep architecture, but reflecting greater richness and complexity. Several changes are seen in Figure 3. An important observation is the progressive reduction in REM sleep through infancy, when important processes of brain maturation are taking place. A stable proportion of about 20% of total sleep time for REM sleep is maintained from childhood forward. We also see a significant reduction in the amount of stage 3 and 4 (delta) sleep from early adult life forward, with almost complete elimination seen in old age. Possible implications and explanations of this will be mentioned below.

However, some possible biases may also be seen in Figure 3. We see a representation of a reduction in total sleep time from early adult life through later adult life. Newer data suggest¹⁷ that such a reduction, if it occurs at all, is not as dramatic as the changes suggested in 1966.¹⁶

Figure 3. Relationship of Rapid Eye Movement (REM) Sleep and Non-REM Sleep Throughout the Human Life^a



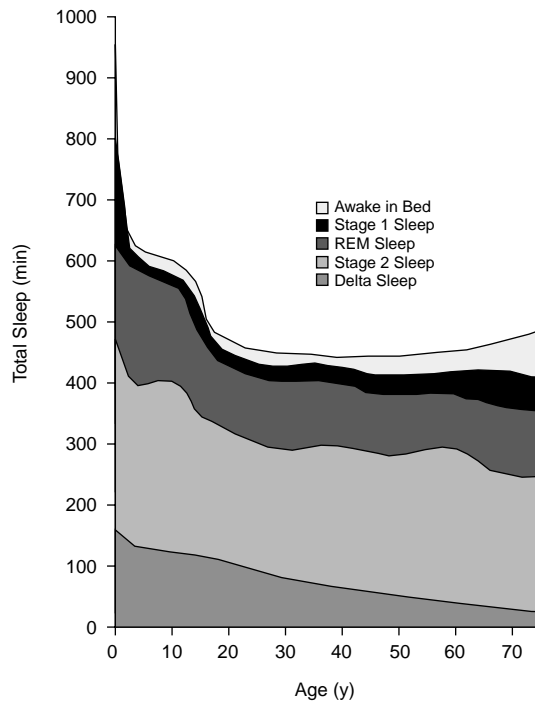
^aReprinted, with permission, from Roffwarg et al.¹⁶ Modified postpublication by Roffwarg on the basis of additional data. Values shown within rapid eye movement sleep area (dark shading) denote percentage of total sleep.

We now recognize, to a greater degree, the importance of considering napping in assessing the total amount of sleep time obtained over the 24-hour cycle. Assessments of the amount of sleep obtained at any stage of adult life must obviously consider naps and periods of “rest” in the daytime, as well as assessing the amount of sleep obtained at night.

Figure 4¹⁸ combines the processes of sleep change and ratios of sleep stages. This graph, in a clear-cut manner, shows both the changes in the relative proportions of the stages and a representation of the relatively minor decline in total sleep time now believed to occur over the later adult years. We also see here the increase in sleep disruptions seen with the aging process, the reduction in sleep efficiency associated with increased time spent awake in bed over the course of the night. The data also reflect the generally accepted perception that there are significant reductions in the amount of delta sleep seen in association with increased age.

Recognizing changes in sleep associated with aging. Other approaches are of relevance as well. For example, is there really a reduction in delta or “deep” sleep associated with the aging process, or is this an anomaly of the criteria used to define delta sleep? It is well recognized that there are reductions in EEG amplitude associated with the aging process. If EEG amplitude is included in a scoring algorithm, as is the case with the R and K criteria, then less delta sleep is scored. However, it has been observed by Feinberg¹⁹ that computer scoring of delta sleep using frequency criteria alone may demonstrate excellent retention of slow-wave sleep, when visual scoring using amplitude criteria would suggest that little or no delta sleep was present. It may well be that using only amplitude criteria, or even using combinations of amplitude and frequency

Figure 4. Development of Sleep Over a Lifetime^a

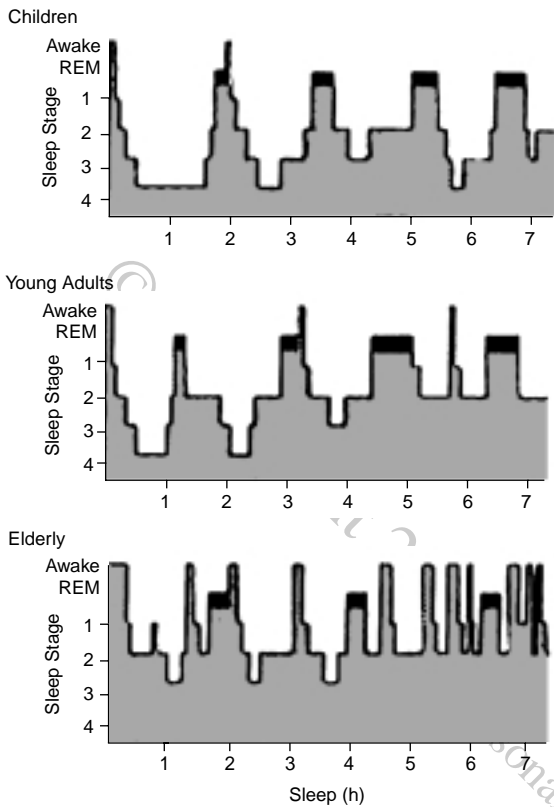


^aReprinted, with permission, from Williams et al.¹⁸ Abbreviation: REM = rapid eye movement.

criteria, as is typically done in visual scoring, may not accurately describe the sleep of aging individuals and may give short shrift to the amount of delta sleep that may be preserved in some older individuals.

Figure 5²⁰ provides another perspective on changes in sleep associated with the aging process. One of the strengths of sleep hypnograms is that they can give us very good representations of sleep continuity. Figure 5 presents typical hypnograms of children, young adults, and the elderly. Several points are of relevance. Reductions are shown in the amount of delta sleep from childhood to adult life and from adult life to old age, reflecting loss of delta sleep by visual scoring. We also see that it is normal for some arousals from sleep to occur in adult life. Although specific sleep pathologies that may lead to awakenings may be seen in the polysomnogram of individuals with insomnia, including periodic limb movements, spontaneous arousal, and sleep apnea, one of the differences between the sleep of the healthy individual and the individual with insomnia relates not to the occurrence of the arousal but to the response to the awakening when it occurs. Does the individual, when he or she awakens, simply roll over and fall back sleep, or does he or she feel a need to look at the clock, leading to greater tendencies to arousal? The individual with insomnia often makes excessive and counterproductive efforts to return to sleep, ruminates about the impact of disturbed sleep on next-day function, and

Figure 5. Typical Sleep Hypnograms for Children, Young Adults, and Elderly Individuals^a



^aReprinted, with permission, from Kales and Kales.²⁰ Abbreviation: REM = rapid eye movement.

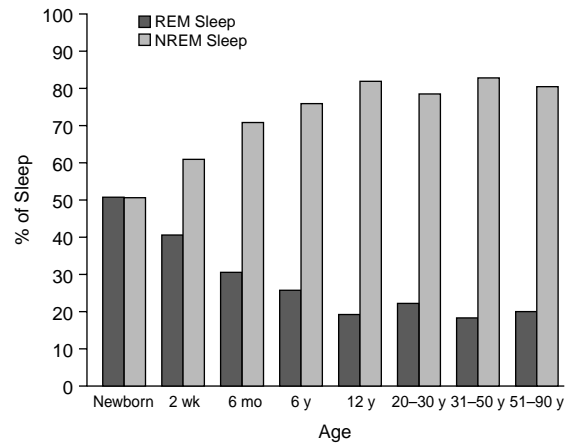
further interferes with natural tendencies to return to sleep after awakening.

Figure 5 illustrates other changes in sleep often seen in the hypnogram of the elderly subject. There is a reduction in total sleep time, with increased time spent awake. This finding may reflect issues in circadian physiology with a tendency to an advanced sleep phase and greater wakefulness toward morning. It may reflect primary sleep disorders such as periodic limb movements in sleep or sleep apnea, medical disorders leading to pain or excessive arousal, or the consequences of napping and dozing at other hours of the day, with reduced sleep drive at night as a result.

The role of new technology. In Figure 6, we see a presentation of ratios of sleep stages. This may be informative about changing processes of sleep-related brain activity, but it tells us little about what is happening in terms of critical duration, depth, or continuity of sleep.

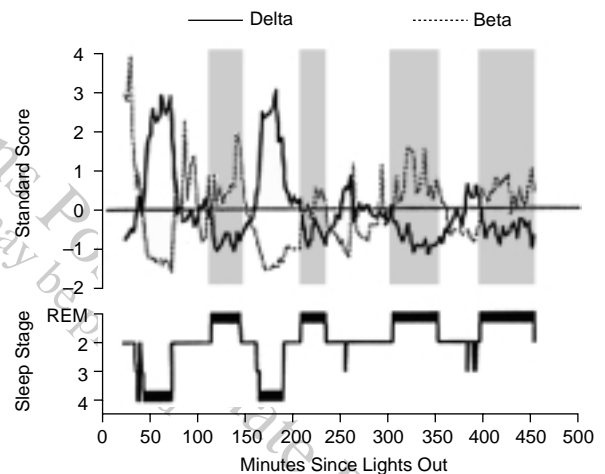
New technologies have provided us with increased capacities to understand sleep using new computer-generated analyses. Figure 7²¹ provides a representation of the power of delta and beta over the course of the night presented alongside a typical sleep hypnogram. We see that there is a large degree of agreement between the power analysis and

Figure 6. Percentage of Sleep Time Spent in Rapid Eye Movement (REM) and Non-REM (NREM) Sleep Over the Life Cycle^a



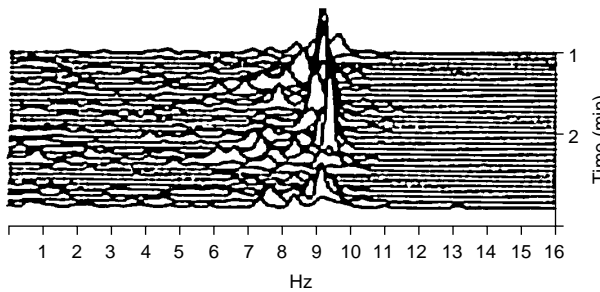
^aReprinted, with permission, from Roffwarg et al.¹⁶

Figure 7. Concordance Between a Computer-Generated Power Analysis of Sleep (top) and a Conventional Sleep Hypnogram (bottom)^a



^aReprinted, with permission, from Feinberg.²¹ Abbreviation: REM = rapid eye movement. Shaded areas designate periods of REM sleep.

more classical sleep scoring data. More importantly, we may obtain important additional information from these types of representations that inform us more about shifts in levels of activity over the course of the night that, in fact, may more accurately describe true sleep physiology. For example, periods scored as the same with regard to sleep stage may differ dramatically in terms of delta or beta power seen. The capacity of computers to supply additional information of this type should provide us with important alternate systems to analyze and understand sleep architecture and physiology.

Figure 8. Compressed Spectral Array Showing Alpha Rhythm^a

^aReprinted, with permission, from Bickford.²²

Power spectral analyses of the sort seen in Figure 8²² hold great promise. Although they are complex and harder to read and interpret than sleep hypnograms, they allow objective description of periods of sleep and objective comparisons between sections of the night or between individuals with regard to sleep EEG characteristics. Although used up to this point primarily in research, they certainly hold promise for the future. These techniques should provide us with better information about disruption of sleep and the impact and characteristics of microarousals and other sleep abnormalities currently not well described in our typical systems of sleep scoring.

THE PAST AS TUTOR OF FUTURE UNDERSTANDINGS OF SLEEP

Our current physiologic “cosmology” relies on such concepts as neurotransmitters and neurochemistry, molecular biology and genetics, and circadian factors to explain regulation of sleep. Although great progress has obviously been made in many areas, we should remain cautious about our current knowledge; yesterday’s “science” may provide today’s humorous observations on the follies of the past.

For example, the book *The Anatomy of Sleep* was published in 1966 by Roche Laboratories.²³ The book, the stated intent of which was to provide physicians with a “review of our ‘other daily life’—sleep,” also provided information about a Roche hypnotic compound, noludar. Of interest to us today are some of the “scientific” statements about sleep made in the publication, which may well have reflected accepted wisdom at the time but which currently would strike us as humorous, if not downright shocking. One was a statement as follows: “When a sleeper is snoring, he isn’t dreaming. The rule is sufficiently reliable to encourage a tormented bedfellow to prod the snorer awake without fear of interrupting some fascinating dream.”^{23(p73)} Quite obviously, we now know that snoring can most certainly take place in REM sleep, and for many individuals tendencies to snoring and sleep apnea are much greater in REM than in NREM sleep.

Even more striking was this description of snoring: “If one were permitted to pick an affliction to suffer from, snoring would be near the top of the list. It causes no health injury. It causes no discomfort to the patient, who seems to enjoy it hugely. The patient only knows of his affliction through hearsay evidence. All the damage, which can be severe, is inflicted on others within earshot.”^{23(pp82–83)} We appreciate, of course, the importance of snoring now as a symptom of sleep apnea. Sleep apnea has obviously been present throughout history. Charles Dickens gives us an excellent description of sleep apnea in his characterization of “Joe, the fat boy,” in his *Pickwick Papers*, published in 1836. Despite this recognition, sleep apnea was not recognized as a disorder until its first descriptions, made essentially simultaneously by groups in Germany and France, were published in 1965.^{24,25} The level of ignorance that existed about snoring and its role as a sentinel symptom of a serious medical and sleep disorder for such a period of time may seem inconceivable to us today, but we can only speculate about how our colleagues in the future may assess our current perceptions of sleep physiology and sleep architecture.

What does the future hold for us in terms of physiologic measures of sleep? Performance-driven measures may be of greater relevance in assessing impact of disturbed sleep than are the static measures that we are currently using. For example, we are able to obtain data of much greater relevance with regard to cardiac function through a technique such as an exercise tolerance test than we obtain from a simple (and static) electrocardiogram. It may well be possible that use of dynamic techniques of this sort, i.e., assessing the impact of sleep on normative daytime function, may be available to us in the future. We would also hope that our capacity to observe some of the disturbances that we may see in the polysomnogram but that are not yet reflected in our sleep-stage scoring may increase. These disturbances may be better assessed by power spectral analyses or other techniques or by techniques that may look, to a greater degree, at measures of alertness, vigilance, reaction time, memory, and other such parameters that may be assessed in a specific and reliable fashion the next day.

SUMMARY

In summary, concepts of sleep architecture clearly have relevance in our understanding of sleep, particularly in describing sleep disturbances that may be seen in insomnia. These concepts are of clear relevance with regard to insomnia. Pathologies in sleep architecture seen in insomnia patients, which are correlated with their subjective complaints, are corrected by hypnotic agents, with improvements in subjective and objective sleep elements. There are clear limitations to the utility of these techniques, and we are likely in the future to be using other techniques and

systems, some of which perhaps have yet to be developed. Among these, we can expect to yield the best data from methods that are not disruptive of sleep processes, that allow computerized analysis of EEG and other sleep parameters, and that will better describe sleep and the consequences of inadequate sleep from functional perspectives.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

REFERENCES

1. Freud S. The psychology of the dream process. In: The Standard Edition of the Complete Psychological Works of Sigmund Freud. London, England: The Hogarth Press; 1953:608
2. Berger H. Uber das Elektroenkephalogramm des Menschen. *J Psychol Neurol* 1930;40:160–170
3. Loomis A, Harvey E, Hobart G. Cerebral states during sleep as measured by human brain potentials. *J Exp Psychol* 1937;21:127–144
4. Kleitman N. *Sleep and Wakefulness*. Chicago, Ill: University of Chicago Press; 1939
5. Aserinsky E, Kleitman N. Regularly occurring periods of eye motility and concomitant phenomena, during sleep. *Science* 1953;118:273–274
6. Rechtschaffen A, Kales A, eds. *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*. Los Angeles, Calif: UCLA Brain Information Service/Brain Research Institute; 1968
7. Dement W, Kleitman N. Cyclic variations in EEG amplitude during sleep and their relation to eye movements, body motility and dreaming. *Clin Neurophysiol* 1957;9:673–690
8. McCall V, Edinger J. Subjective total insomnia: an example of sleep state misperception. *Sleep* 1992;15:71–73
9. Carskadon M, Dement W, Mitler M, et al. Self-report versus sleep laboratory findings in 122 drug-free subjects with complaints of insomnia. *Am J Psychiatry* 1976;113:1382–1388
10. Nowell P, Mazumdar S, Buysse D, et al. Benzodiazapines and zolpidem for chronic insomnia. *JAMA* 1997;278:2170–2177
11. Gillin J, Byerley W. The diagnosis and management of insomnia. *N Engl J Med* 1990;322:239–248
12. Steens R, Pouliot Z, Millar T, et al. Effects of zolpidem and triazolam on sleep and respiration in mild to moderate chronic obstructive pulmonary disease. *Sleep* 1993;16:318–326
13. Erman M, Scharf M. Effects of zolpidem in patients with obstructive sleep apnea. *Sleep Res* 1998;77
14. Mitler M, Seidel W, Van Den Hoed J, et al. Comparative hypnotic effects of flurazepam, triazolam and placebo: a long-term simultaneous nighttime and daytime study. *J Clin Psychopharmacol* 1984;4:2–13
15. Danjou P, Paty I, Fruncillo R, et al. A comparison of the residual effects of zaleplon and zolpidem administration 5 to 2 h before awakening. *J Clin Pharmacol* 1999;48:367–374
16. Roffwarg H, Muzio J, Dement W. Ontogenetic development of the human sleep-dream cycle. *Science* 1966;152:604–619
17. Bliwise D. Normal aging. In: Kryger M, Roth T, Dement W, eds. *Principles and Practice of Sleep Medicine*. Philadelphia, Pa: WB Saunders Co; 2000:26–42
18. Williams RL, Karacan I, Hirsch CJ. *Electroencephalography (EEG) of Human Sleep: Clinical Applications*. New York, NY: John Wiley & Sons; 1974
19. Feinberg I, Hibi S, Carlson V. Changes in EEG amplitude during sleep with age. In: Nandy K, Sherwin I, eds. *The Aging Brain and Senile Dementia*. New York, NY: Plenum Press; 1977:85–98
20. Kales A, Kales JD. Sleep disorders: recent findings in the diagnosis and treatment of disturbed sleep. *N Engl J Med* 1974;290:487–499
21. Feinberg I. Cycles of sleep across the night. In: Carskadon MA, ed. *Encyclopedia of Sleep and Dreaming*. New York, NY: Macmillan; 1993:160
22. Bickford RG. Newer methods of recording and analyzing EEGs. In: Klass DW, Daly DD, eds. *Current Practice of Clinical Electroencephalography*. New York, NY: Raven Press; 1979:451–479
23. *The Anatomy of Sleep*. Nutley, NJ: Roche Laboratories, Division of Hoffman-LaRoche; 1966
24. Gastaut H, Tassinari C, Duron B. Etude polygraphique des manifestations episodiques (hypniques et respiratoires) du syndrome de Pickwick. *Rev Neurol* 1965;14:586–594
25. Jung R, Kahlo W. Neurophysiological studies of abnormal night sleep and the pickwickian syndrome. *Prog Brain Res* 1965;18:140–159