Methodology

Max Hirshkowitz

100

Monitoring and Staging Human Sleep

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The goal of this chapter is to summarize the procedures for monitoring and evaluating sleep in the laboratory setting. This material will not substitute for the standard manual; rather, one hopes it will be complementary. After recommended techniques and procedures are summarized, a few problematic areas are discussed briefly.

Although it is possible to monitor continuously and concurrently the activity of dozens of systems during sleep, one need measure just three systems to assess sleep according to standard criteria.[1] This standard system of sleep recording and staging criteria is firmly rooted in the U.S. sleep research tradition, and although certain of its criteria have been challenged in recent years, it is the only system established by a consensus of experts.

Among the earliest descriptions of electroencephalographic (EEG) activity during sleep were those from the laboratory of Loomis et al.[2] These authors described five stages of sleep but failed to distinguish rapid eye movement (REM) sleep. Not until the landmark work of Kleitman's group at the University of Chicago was REM sleep described,[3] a description made possible by the addition of electro-oculography (EOG) to the recording paradigm. The first comprehensive description of the nocturnal pattern of nonrapid eye movement (NREM) and REM sleep in human beings[4] remains the foundation of modern human sleep research and represents one of the most outstanding scientific achievements of the 20th century. The standard sleep staging system[1] modified the EEG and EOG categorizations of Dement and Kleitman[4] primarily by adding electromyography (EMG). The addition of EMG to the criteria was based on the research of Berger[5] in human beings and Jouvet[6] in cats, which linked muscle atonia with REM sleep. The EMG provided a more stable marker for REM sleep than the intermittent bursts of rapid eye movements.

PROCEDURES FOR MONITORING SLEEP

The EEG is the core measurement of polysomnography. The four stages of NREM sleep are distinguished from each other principally along this dimension.

Electroencephalogram

Application. The reliable recording of EEG begins with accurate measurement of the skull according to the international 10–20 system of electrode placement.[7] A skilled technologist can make the requisite measurements in 10 min. The "eyeball" or "rule-of-thumb" placement of EEG electrodes is not recommended because of the marked variability of electrode locations

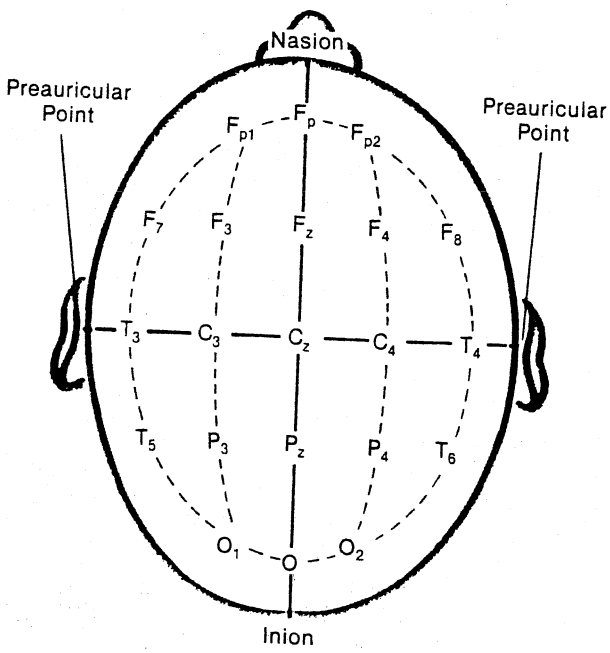

Figure 100–1. Schematic diagram showing measurements for the 10–20 electrode placement system. Measurements are made at 10 and 20% of the distances from inion to nasion, from left to right preauricular points, and around the circumference of the head. Intersecting points denote electrode placements. The most common placements for recording the electroencephalogram (EEG) during sleep are C3 (left central), C4 (right central), O1 (left occipital), and O2 (right occipital). (Redrawn from Harner PF, Sannit T. A Review of the International Ten-Twenty System of Electrode Placement. Quincy, Mass: Grass Instrument Company; 1974.)

such practices engender, regardless of the technologist's skills.

Figure 100–1 illustrates the 10–20 placement system, by which a grid is placed over the skull and points of intersection denote electrode placement locations. The name of the system derives from measurements made at intervals of 10 or 20% of the total distance between landmarks. The four landmarks of the system are the nasion, inion (external occipital protuberance), and left and right preauricular points. Thus, the measurements are specific to each individual.

After measurements are made, the hair is separated and the scalp is cleaned in preparation for electrode application. In the past, technologists have used coarse-grained compounds to abrade the scalp, enabling better signal conduction. This practice has recently been discouraged in response to the increased risk of infection from bloodborne viruses.[8] Thorough cleansing and removal of dead skin layers by brisk rubbing with gauze are generally sufficient to ensure adequate conduction when the electrode is applied over a good conducting medium. The EEG electrodes for overnight sleep studies are generally attached to the scalp using small patches of gauze soaked in collodion and dried with compressed air. The conducting medium may be added through a small hole in the electrode cup, or if it is placed in the cup before application, an airtight seal will prevent evaporation for at least 24 to 36 h.

Derivations. The standard manual[1] recommends referential recording of one EEG lead, either C3 or C4, referenced to an indifferent auricularly placed electrode on the contralateral mastoid or ear lobe: hence C3/A2 or C4/A1. The recommended sleep staging criteria, therefore, are intended to be used with this single, central EEG lead. The recommendations of the original committee acknowledged that use of a single EEG channel was largely an economic issue for most laboratories, which at that time were limited to eight-channel recording systems on which two subjects were generally recorded simultaneously. Nevertheless, this economically dictated approach has proved to be a remarkably robust system.

Sleep stage scoring does not require measurement of focal EEG activity or regional comparisons, as might be performed in an EEG laboratory. Rather, all of the EEG waveforms used to distinguish sleep stages are well visualized at C3 or C4, particularly when signal amplitudes are optimized, with the relatively large interelectrode distance afforded by a contralateral reference. Thus, vertex sharp waves and K complexes, which are maximal over the vertex, are clearly evident at C3 and C4; high-voltage slow waves characteristic of deep NREM sleep are seen maximally in frontal regions yet show clearly on central derivations; alpha rhythm, by contrast, is maximal over the occipital poles but can be characterized centrally in most human beings.[9, 10]

Therefore, only C3/A2 or C4/A1 is used in the standard assessment of sleep stages. Many laboratories, however, routinely record an occipital EEG (usually O1/A2 or O2/A1) as an adjunct to the central EEG, particularly for assessing sleep onset or arousals during sleep. Certain laboratories also routinely record from frontal placements. When the latter procedure is used for sleep staging, however, there is a tendency to observe a somewhat greater quantity of the deep NREM sleep stages (stages 3 and 4); therefore, such use should be documented in any published reports.

Electro-Oculogram

There are two primary reasons to record eye movement activity during sleep. The most obvious is to record the cardinal sign of REM sleep—the phasic bursts of rapid eye movements—which is an essential sleep stage scoring criterion. In addition, the onset of sleep in most human beings is heralded or accompanied by slow, rolling eye movements, which also occur with transitions to stage 1 during the night. Although these slow eye movements (SEMs) are not essential to sleep staging, they often provide very useful information.

The EOG recordings are based on the small electropotential difference from the front to the back of the eye. The cornea is positive with respect to the retina. Thus, the eyeball exists in the head as a potential field within a volume conductor. Because of this essentially constant potential difference, movement of the eyes can be measured from electrodes placed beside the eyes. An electrode nearest the cornea will register a positive potential; an electrode nearest the retina will

register a negative potential. As the eye moves, the positions of the cornea and retina change relative to the fixed position of the electrode, and a potential change will register as a pen deflection at the polysomnograph.

Application. Standard EOG placements include the right outer canthus (ROC) and the left outer canthus (LOC). According to the standard manual,[1] the EOG electrodes should be offset from horizontal, one slightly above and one slightly below the horizontal plane. In this manner, the electrodes can detect horizontal and vertical eye movements. The EOG electrodes are usually applied with tape to a skin surface that has been thoroughly cleansed. An airtight seal over the electrode will protect the conductivity of the electrode jelly for approximately 24 h. The collodion electrode application technique is greatly discouraged for EOG leads because of the risk of splashing collodion into the eyes.

Derivations. The standard manual[1] recommends continuous referential recording of two EOG leads: one outer canthus placement referred to the auricular reference on the opposite side and the other to the same auricular reference (e.g., ROC/A1 and LOC/A1). Certain laboratories[11] routinely use a contralateral reference for each outer canthus placement (ROC/A1 and LOC/A2). In the latter case, the contralateral references maximize the signal amplitude for both EOGs and equalize the amplitudes of pen deflections for conjugate eye movements. Either technique provides the capability to distinguish eye movements from electrode artifact. For example, in a montage recording ROC/A1 on one channel and LOC/A2 on another, conjugate eye movements will register as out-of-phase pen deflections; EEG activity reflected in the EOG channels (e.g., K complexes) will be seen as in-phase deflections; and electrode artifacts will register in phase or in only one channel.

When a major goal of an experiment is to determine more precisely the direction of eye movements, the EOG may be simultaneously recorded from horizontal and vertical placements. Thus, in addition to placements on the outer canthi, electrodes would be placed supraorbitally and infraorbitally. For exact determination of eye position, direct current (DC) recordings are recommended.

Electromyogram

In a standard polysomnographic recording, the EMG from muscles beneath the chin is used as a criterion for staging REM sleep.[1] The EMG recordings from other muscle groups are sometimes used to assess certain sleep disorders. For example, the anterior tibialis EMG is important to evaluate patients who have periodic movements in sleep. The intercostal EMG may be used to monitor respiratory effort. Most EMG recordings during sleep require taping electrodes to the skin over the muscle group of interest.

Application. Three electrodes are placed beneath the chin, overlying the mentalis/submentalis muscles. These placements, rather than others, are recommended for the sake of convenience. The chin is very accessible, and the electrode wires can be drawn together with the others to form a bundle or "pony tail" at the back of the head. As in preparation for the EEG and EOG leads, the skin is thoroughly cleansed of oils and dead skin cells before applying the electrodes, which are generally secured with tape. Particularly in the case of a patient with a beard, the EMG electrodes may be affixed using a collodion-soaked gauze pad in the manner of the EEG leads.

Derivations. The EMG is recorded bipolarly. Any combination of the three placements can be used; the pair selected should produce the record of highest quality. The primary reason for using three electrodes (even though only two are recorded at any given time) is to ensure that there is always a back-up electrode in case of failure of one placement. Availability of a back-up is important, especially if electrodes remain in place during the daytime when subjects are eating and talking. To monitor bruxism, one EMG may be offset to a location over the masseter muscle.

General Considerations for Recording Sleep

A minimal four-channel montage for recording sleep is shown in Table 100–1. If channels are limited, it is possible to use a single EOG channel, although this practice is discouraged. If more channels can be devoted to the sleep portion of the recording, an occipital EEG will be the most helpful addition. When limited to four sleep channels, some laboratories begin a night's recording with a central and an occipital EEG, a single EOG, and an EMG. After sleep onset, the occipital EEG is replaced with the second EOG.[11] Depending on the purpose of the recording, other selected parameters will be added to the montage to record respiration, heart rate, blood pressure, esophageal pH, penile circumference, or any of the many other available systems. To correlate other events with sleep stages, it is most convenient to output all signals to a single device. When more than one recording device is used, it is helpful if they are linked to a single time-code generator.

Most sleep laboratories use a standard chart paper speed of 10 or 15 mm/sec. Slower speeds are discouraged because clear visualization of alpha rhythm and

Table 100–1. MONTAGE FOR MONITORING SLEEP STATES

Parameter	Derivation	Back-Up or Option
EEG	C3/A2	C4/A1
EOG	ROC/A1 and LOC/A1	ROC/A1 and LOC/A2
EMG	Mentalis/submentalis	
If additional channels are available, add the following:		
EEG	O1/A2	O2/A1
EOG	Infraorbital/supraorbital	

sleep spindles becomes extremely difficult. Faster paper speeds are unusual because of the generally prohibitive expense of the recording chart paper. A sensitivity that gives a pen deflection of 7.5 or 10.0 mm for a 50-μV signal is recommended for the EEG and EOG channels. The chin EMG amplification is often adjusted after the recording has begun so that an acceptable EMG recording is obtained. A known calibration of the central EEG leads is *essential* because of the amplitude criterion for scoring NREM stage 3 and 4 sleep. A calibration of 50 μV/cm is common. Greater amplification of the EEG may result in pen blocking during slow-wave sleep (stages 3 and 4), especially in younger subjects. Lower amplification may result in difficulty observing small-amplitude sleep spindles.

Electroencephalographic filtering should allow suitable visualization of a fairly wide range of signals, from slow waves (2 cps or less) to sleep spindles (12 to 14 cps). A high-frequency filter setting in the range of 30 to 35 cps will generally pass through the essential waveforms, while minimizing high-frequency (e.g., EMG) interference. A time constant of 0.3 sec or slower (corresponding to a half-amplitude low-frequency filter setting of about 0.3 cps) is recommended to ensure adequate coverage of slow wave activity.

The same settings are recommended for EOG channels. This filtering will pass both the rapid eye movements essential to scoring REM sleep and the SEMs characteristic of sleep onset and transitional stage 1 sleep. A faster time constant has been used in certain laboratories to reduce the "contamination" of EOG by EEG signals. In slow-wave (stages 3 and 4) sleep, however, the EEG activity seen in the EOG channels (with a slow time constant) tends to have fewer overriding fast components than the central leads and may therefore be helpful in distinguishing the slow EEG components. Thus, the slower time constant for EOGs may be doubly helpful.

The EMG is generally recorded with a much higher setting on both high- and low-pass filters. A low-pass setting of 70 or 75 cps is common (with notch filtering of alternating current [AC] interference, e.g., 60 Hz). High-pass filtering at 10 cps (time constant = 0.015 sec) is useful to prevent slow signals from interfering with the EMG tracing. The standard manual recommends a time constant for EMG of 0.1 sec or faster.[1] The absolute amplitude of EMG activity is not relevant to polysomnography; the emphasis, rather, is on relative changes in EMG amplitude. Thus, the EMG level is adjusted at the start of the record to provide an amplitude permitting such comparisons. An amplification of 20 μV/cm at the start of the recording will usually approximate a reasonable EMG level.

A number of special cases may require modification of the sensitivity, filter, and time constant settings just described. In certain patients (especially older individuals), the amplitude of the EEG using the standard gain may be so small that the record is extremely difficult to evaluate. The gain may be increased so that a 50-μV pulse gives a pen deflection of 15 mm. By contrast, the amplitude of the EEG in some young children is so great that the pen sweep is not large enough to register the signal. In this instance, the sensitivity of EEG channels (and EOG channels) may be reduced so that a 50-μV pulse causes a pen deflection of 5 mm.

The EEG and EOG channels may also pick up a very low-frequency artifact related to sweat. If extreme, "sweat artifact" can make the record virtually unscorable. When a correction cannot be made by re-referencing or by lowering the room temperature, the low-frequency cutoff may be set at 1.0 cps (time constant = 0.1 sec). This step is recommended only in extreme cases in adults; in children, sweat artifact usually does not need to be extreme to justify changing the low-frequency filter because children have such pervasive slow wave activity in stages 3 and 4 sleep. One should never use the 5-cps low-frequency cutoff setting for the EEG because the slow frequencies of stage 3 and 4 sleep would be lost entirely.

A sleep tracing requires constant vigilance during the night, and a key concern is that the technologist stays awake and alert. The recording must be observed frequently to check for paper jams, ink clogs, recording artifacts, changes in pen alignment, and so forth. This requirement for technologist vigilance makes the process of laboratory sleep recording a labor-intensive procedure; however, it also eliminates the necessity of retesting because of lost data, which may occur when out-of-laboratory procedures are used.

PROCEDURES FOR STAGING SLEEP

General Considerations

The standard sleep staging manual[1] provides detailed guidelines and criteria for staging normal human sleep. The following material does not supersede the manual but is intended to be supplementary.

Several general concepts, referring primarily to the EEG, are helpful when one approaches sleep stage scoring. It should first be noted that the sleep research community has adopted the EEG convention of "negative up," which simply means that a signal of negative polarity is shown as an upward pen deflection. Second, a number of the standard guidelines refer to the frequency of the EEG waves. Frequency is measured as cycles (each cycle is the complete series of potential changes before the series repeats) per second. A few common EEG frequency bands are as follows:

1. Alpha rhythm: 8 to 13 cps
2. Beta rhythm: more than 13 cps
3. Delta rhythm: less than 4 cps
4. Theta rhythm: 4 to 7 cps

The amplitude measures used in sleep staging are taken from trough to peak (or peak to trough) of the wave, rather than from baseline or zero crossing to peak or trough.

When a sleep recording is scored, it is customary to divide the chart into convenient segments and to assign a sleep stage value to each segment or epoch. The most common epoch length is 30 or 20 sec, which

Table 100–2. PARTIAL LISTING OF EVENTS THAT MAY BE CODED WITHIN OR ACROSS EPOCHS

Body movement	Penile tumescence
Movement arousal	T_{up}
Transient arousal	T_{max}
Microsleep episodes	T_{down}
K-alpha complex	Heart rate irregularities
Esophageal pH abnormalities	Asystole
Respiratory abnormalities	Premature ventricular contraction (PVC)
Apnea	Premature atrial contraction (PAC)
Obstructive	Tachycardia
Central	Bradycardia
Mixed	Oxygen saturation
Hypopnea (usually ≥10 sec)	Below 90%
Obstructive	Below 80%
Central	REM phasic events
Mixed	Twitches
Paradoxical respiration	Rapid eye movements
Cheyne-Stokes respiration	Middle ear muscle activity
Periodic breathing	Periorbital integrated potentials
Periodic movements	
With arousal	
Without arousal	

corresponds to a single page of chart paper 300 mm wide recorded with a chart speed of 10 or 15 mm/sec. A 1-min scoring epoch has also been used (see particularly Williams et al.[12]), although such a long epoch may overlook stage changes of relatively short duration.[13] A scoring epoch shorter than 20 sec is considered too tedious by most groups, although epochs as short as 3 sec have been used for specific research purposes.

Each epoch is assigned a score that most appropriately characterizes the predominant pattern occurring during that interval. Thus, the purpose of epoch staging is to determine the single descriptive factor that most fully characterizes the epoch. Any number of additional codes may be used to denote activities or events occurring within (or across) an epoch. Thus, for example, the standard manual describes "movement arousals," which are short-lived events occurring within an epoch but not descriptive of the majority of the epoch. With the increasing application of polysomnography to clinical assessments, the variety of possible events to be evaluated has grown markedly. Table 100–2 gives a partial listing of events that are coded by various laboratories. To date, these events have usually been defined within each laboratory because standard consensus descriptions are generally lacking. Laboratories typically select those events that are of local experimental or clinical relevance. Event coding is an extremely valuable adjunct to sleep staging but is not a substitute for sleep staging.

Sleep Staging in Normal Adult Human Beings

The following material summarizes the criteria described in the standard manual[1] for staging normal human sleep. Although these criteria apply most specifically to adults, they have also been used to characterize sleep in children and adolescents.[14, 15] A separate set of criteria, however, is generally deemed necessary in newborns[16] and older infants.[17] The standard sleep staging criteria in adults, according to the three electrographic parameters, are outlined in Table 100–3 and described below.

Relaxed Wakefulness. The majority of human beings show an EEG of rhythmic alpha activity (in the range of 8 to 13 cps) when relaxed with the eyes closed (Fig. 100–2). This activity is maximal occipitally but also often occurs centrally. This rhythmic EEG pattern attenuates with attention, as well as when the eyes are open (Fig. 100–3), at which time the waking EEG pattern is best characterized as one of relatively low voltage and mixed frequency. In an excessively sleepy individual, rhythmic alpha activity may be present when the eyes are open and may attenuate with eye closure; in this case, alpha attenuation is related to the intrusion of stage 1 sleep.

When a person is awake, control of eye movements is voluntary. The waking EOG tracing generally consists of rapid eye movements and eye blinks when the eyes are open and few or no eye movements with the eyes closed. Involuntary slow, rolling eye movements (with eyes closed) often characterize the EOG in the seconds to minutes preceding the EEG change to stage 1 sleep.

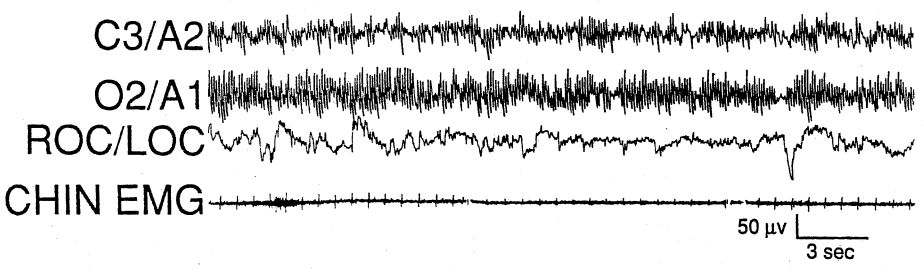

Figure 100–2. Rhythmic EEG alpha activity is clearly evident in the C3/A2 and O2/A1 tracings of this young adult male volunteer who is awake with his eyes closed. Figures 100–2 to 100–7 and 100–9 to 100–13 are all taken from an overnight recording of a 19-year-old normal male volunteer. All leads were recorded on a Grass Instruments Company Model 78 polygraph. The central and occipital EEGs and the electro-oculograms (EOGs) used a low-frequency cutoff of 0.3 cps, a high-frequency cutoff of 30 cps, and sensitivity of 50 µV/cm. The electromyogram (EMG) was recorded with a low-frequency cutoff of 10 cps, high-frequency cutoff of 60 cps, and sensitivity of 20 µV/cm. Paper speed was 10 mm/sec. In Figures 100–2 to 100–5, the EOG is monitored with a single lead (ROC/LOC). In Figures 100–9 to 100–13, the occipital tracing has been dropped, and the EOG is recorded from two leads, ROC/A1 and LOC/A2. (See text for comments on the latter procedure.)

Table 100–3. OUTLINE OF SLEEP SCORING CRITERIA ACCORDING TO STANDARD MANUAL

Stage/State	EEG	EOG	EMG
Relaxed Wakefulness	**Eyes closed:** rhythmic alpha (8–13 cps); prominent in occipital; attenuates with attention **Eyes open:** relatively low voltage, mixed frequency	Voluntary control; REMs or none; blinks; SEMs when drowsy	Tonic activity, relatively high; voluntary movement
NREM			
Stage 1	Relatively low voltage, mixed frequency May be theta (3–7 cps) activity with greater amplitude Vertex sharp waves Synchronous high-voltage theta bursts in children	SEMs	Tonic activity, may be slight decrease from waking
Stage 2	**Background:** relatively low voltage, mixed frequency **Sleep spindles:** waxing, waning, 12–14 cps (≥0.5 sec) **K complex:** negative sharp wave followed immediately by slower positive component (≥0.5 sec); spindles may ride on Ks; Ks maximal in vertex; spontaneous or in response to sound	Occasionally SEMs near sleep onset	Tonic activity, low level
Stage 3	≥20 ≤50% high amplitude (>75 μV), slow frequency (≤2 cps); maximal in frontal	None, picks up EEG	Tonic activity, low level
Stage 4	>50% high amplitude, slow frequency	None, picks up EEG	Tonic activity, low level
REM	Relatively low voltage, mixed frequency Sawtooth waves Theta activity; slow alpha	Phasic REMs	Tonic suppression; phasic twitches
Movement Time	Obscured	Obscured	Very high activity
Anomalous Sleep*	Similar to REM	Phasic REMs	Tonic activity; phasic twitches

*Described in reference 44.

Modified from 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.

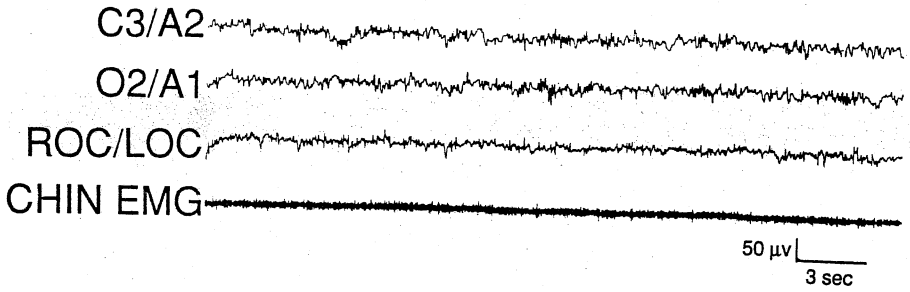

Figure 100–3. Attenuation of waking EEG alpha activity with eyes open is illustrated in this tracing. Note the characteristic "relatively low-voltage, mixed-frequency" EEG activity.

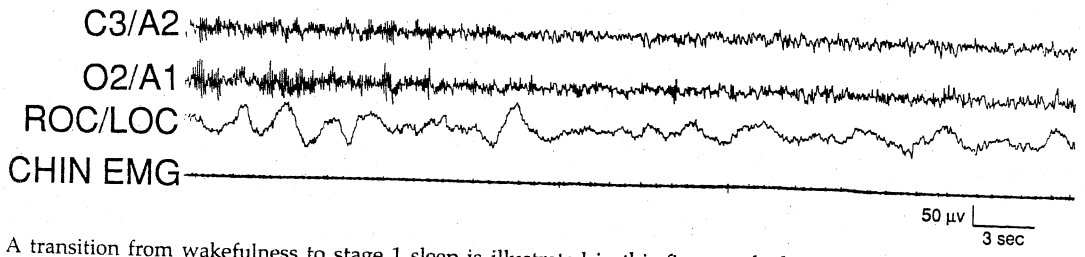

Figure 100–4. A transition from wakefulness to stage 1 sleep is illustrated in this figure, which clearly shows the attenuation of alpha that marks the onset of stage 1 sleep. As described in Figure 100–3 for an EEG of wakefulness with the eyes open, the EEG pattern of stage 1 sleep is described as one of "relatively low voltage, mixed frequency." Note, too, the presence of slow eye movements in the EOG tracing.

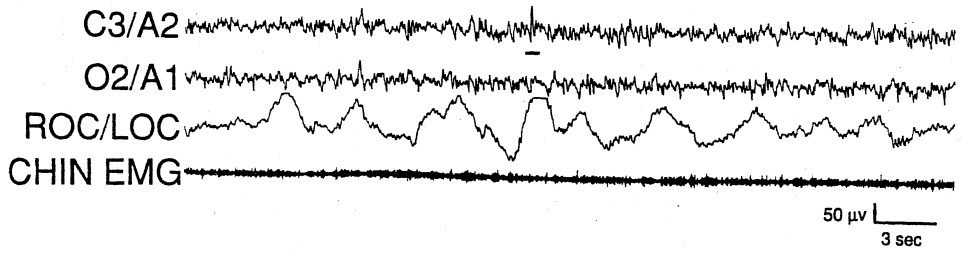

Figure 100–5. Vertex sharp waves are a common feature of the onset of stage 1 sleep. Few were seen in this volunteer, however, although one *(underlined)* is illustrated in this figure. Note that the vertex sharp wave is visible in the C3/A2 lead, but not in the O2/A1 lead, emphasizing localization to the vertex region.

The EMG shows tonic activity of a relatively high level. Voluntary movements produce phasic increases of EMG amplitude. In very relaxed individuals, waking EMG tonus may be indistinguishable from NREM sleep.

NREM Sleep. The four NREM sleep stages are distinguished, as mentioned previously, principally by changes in EEG pattern. The EOG and EMG patterns contribute little to NREM sleep staging, except in the case of transitional stage 1 NREM sleep, in which both may be useful. Therefore, the discussion below will focus on EEG.

Stage 1. The transition from wakefulness to stage 1 sleep (Fig. 100–4) is most clearly visualized on the EEG when the waking pattern has well-defined rhythmic alpha activity. It is for this reason that an occipital derivation is frequently added to the sleep recording montage, because waking alpha is most prominent in this cortical region. The EEG pattern of stage 1 is described as relatively low-voltage, mixed-frequency activity. Especially during stage 1 sleep occurring at the beginning of the night, vertex sharp waves (Fig. 100–5) are common. In addition, the EEG activity with the highest relative amplitude during stage 1 sleep is generally in the theta (3 to 7 cps) range. Bursts of relatively high-voltage, very synchronous theta activity are common during the onset of stage 1 sleep in children and young adolescents (Fig. 100–6).

The SEMs commonly precede the EEG transition to stage 1 sleep from wakefulness. Although the onset of SEMs usually leads the EEG transition by only 1 or 2 min, the lead time may occasionally—particularly in daytime recordings—be as long as 15 min.[18] Slow eye movements are very useful to distinguish stage 1 sleep transitions occurring during stage 2 NREM sleep or REM sleep.

Muscle tone is maintained during all NREM sleep stages and registers as low-amplitude EMG activity. There generally is no discrete change in EMG amplitude in the wake-to-sleep transition, although a gradual diminution of the EMG signal amplitude may occur within moments of the transition. During NREM sleep, the EMG is most helpful for distinguishing movement arousals, which are useful in certain stage change decisions. In addition, a rise in EMG activity often will be the only discrete indicator of a transition to stage 1 sleep within a REM sleep episode (see Fig. 100–12).

Stage 2. The background EEG of stage 2 NREM sleep is a pattern of relatively low-voltage, mixed-frequency activity. Stage 2 is distinguished from stage 1 on the basis of two specific EEG patterns that occur sporadically on this mixed-frequency background: the sleep spindle and K complex (Fig. 100–7). Because these stage 2 defining EEG patterns occur episodically, the standard staging criteria[1] provide for a default to stage 1 sleep if neither a sleep spindle nor a K complex occurs within a 3-min span when the EEG is of relatively low voltage and mixed frequency (the "3-min" rule).

In their most pure presentation, sleep spindles, have a waxing and waning spindle shape (Fig. 100–8), composed of waves in the range of 12 to 14 cps, with a duration of about 0.5 to 1.5 sec.[19] Sleep spindles are a common feature of mammalian sleep, and when recorded using identical techniques, they are indistinguishable, for example, between human beings and cats.[20] Sleep spindle activity occurs during stage 2 sleep, with a frequency of about three to eight spindles per minute in normal adults[21] or insomniac adults,[22] and spindle rate appears to be a fairly stable individual characteristic.[21] "Incipient sleep spindles" may appear near the stage 1 to stage 2 transition early during sleep; however, "the presence of a spindle should not be defined unless it is of at least 0.5 sec duration, i.e., one should be able to count 6 or 7 distinct waves within the half-second period."[1]

From an ontogenetic perspective, sleep spindles in the human being usually develop before age 3 months.[23, 24] In mentally retarded infants, sleep spindles are slower to develop and occur less frequently than

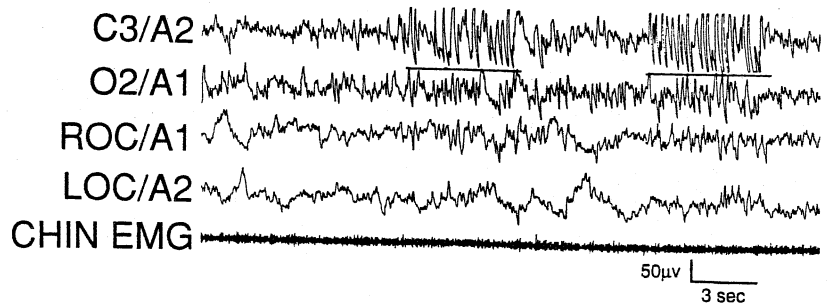

Figure 100–6. Very high-voltage, highly synchronous theta activity *(underlined)* is common during sleep onset stage 1 in children and young adolescents. This phenomenon is illustrated here in a tracing from a 14-year-old male volunteer. (Recording parameters are as described in the legend for Figure 100–2, with the exception that EEGs were recorded with a low-frequency cutoff of 1.0 cps.)

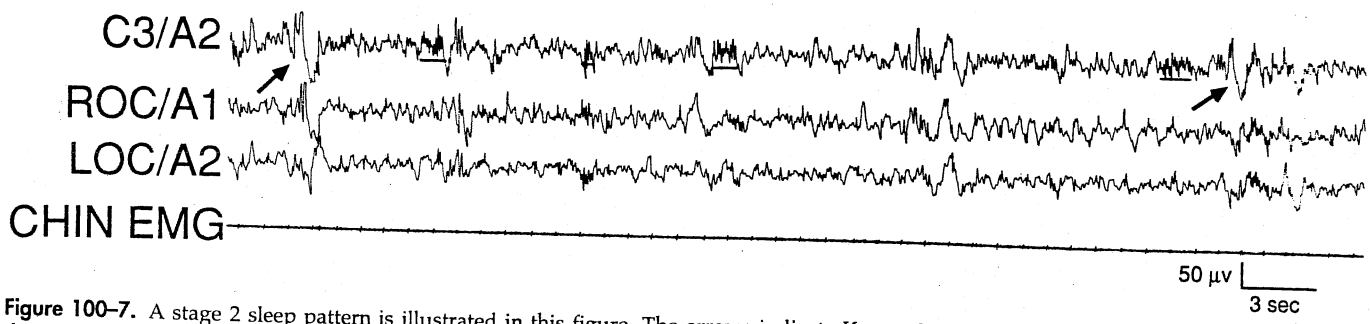

Figure 100–7. A stage 2 sleep pattern is illustrated in this figure. The arrows indicate K complexes, and sleep spindles are underlined. Note that K complexes are seen in the EOG tracings but are distinct from eye movements because the EOG tracings are in phase with one another. The last K complex in this figure illustrates the coincidence of a sleep spindle and a K complex, seen as relative low-voltage activity of spindle frequency (12 to 14 cps) on the trailing portion of the K complex.

in normal infants.[25] In old persons, sleep spindles tend to lose their classic morphology and have a slightly slower frequency, lower amplitude, and shorter duration[26, 27] than in the young adult. Benzodiazepine hypnotics tend to increase the density of sleep spindles in stage 2 sleep.[22, 28]

Sleep spindles* are absent in stage 1 NREM but may occur in REM sleep, particularly in subjects or patients whose sleep has been restricted or fragmented. If a single sleep spindle occurs in the middle of a REM sleep episode, it is not considered to be indicative of a stage change. If, however, two sleep spindles bracket half a scoring epoch or longer with no REMs intervening, the interval between spindles is considered a stage 2 sleep interruption of the REM episode.

The K complex (see Fig. 100–7) is another sleep-specific EEG waveform that is characteristic of stage 2 sleep. This paroxysmal wave complex consists of a "well-delineated negative sharp wave which is immediately followed by a positive component. The total duration of the complex should exceed 0.5 sec."[1] The standard manual provides no amplitude criterion for K complexes. There usually is very little difficulty in discerning K complexes in stage 2 sleep. The following definition used by electroencephalographers for the term *complex* is very helpful when a K complex distinction is in doubt, as may occur in stage 3 and 4 sleep, when it is sometimes difficult to differentiate K complexes from high-voltage slow wave activity. A complex is a "group of two or more waves, clearly distinguished from background activity and occurring with a well-recognized form or recurring with consistent form."[29] A key part of this definition is that the complex is distinct from the ongoing background activity, which makes the K complex in stage 2 very clear, whereas the same morphology embedded within a series of high-voltage, slow wave activity during stage 3 or 4 would probably not stand out from the background.

K complexes are maximal over the vertex. It is very common for spindle activity (12 to 14 cps) to ride over the K complex. In young adults, the typical density of K complexes in stage 2 is about 1 to 3 per minute,[21, 30, 31] although there is considerable individual variability. K complexes occur spontaneously during stage 2 sleep and are also evoked in response to auditory stimuli.

At the beginning of the night, SEMs may infrequently and only very briefly persist after the appearance of sleep spindles and K complexes. Because the EOG channels also register EEG activity, K complexes can reflect on these channels (see Fig. 100–7). They are generally easily distinguished from rapid eye movements because the pens on the two channels deflect in phase and because the central EEG amplitude of a K complex is usually much greater than any EEG activity related to eye movements. The EMG during stage 2 sleep is tonically active, generally at a low amplitude relative to wakefulness.

Stages 3 and 4. The EEG of stage 3 and 4 sleep is defined by the presence of high-voltage slow wave activity (Figs. 100–9 and 100–10). In stage 3 sleep, "at least 20 per cent but not more than 50 per cent of the epoch consists of waves of 2 cps or slower which have amplitudes greater than 75 μV from peak to peak (the difference between the most negative and positive points of the wave)."[1] In stage 4 sleep, such waves predominate (more than 50% of the epoch). Sleep spindles can occur during stages 3 and 4, as can K complexes; however, they are only infrequently distinct from the background EEG activity, particularly in stage 4 sleep. Eye movements do not occur during stage 3 and 4 sleep, although the EOG will register the high-voltage slow wave activity. The EMG during stages 3 and 4 is tonically active, although the tracing may occasionally achieve very low levels, nearly indistinguishable from that of REM sleep.

REM Sleep. Staging REM sleep requires the coinci-

*The term *K complex* may be substituted for *sleep spindle* throughout this paragraph.

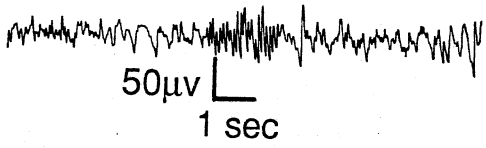

Figure 100–8. A sleep spindle from stage 2 sleep in a normal 16-year-old adolescent girl is illustrated in this figure. The activity is grossly spindle shaped, with waxing and waning amplitude. Elderly volunteers and many patients with sleep disorders no longer have spindles with this morphology. The "spindles" tend to be shorter and of lower amplitude in such individuals.

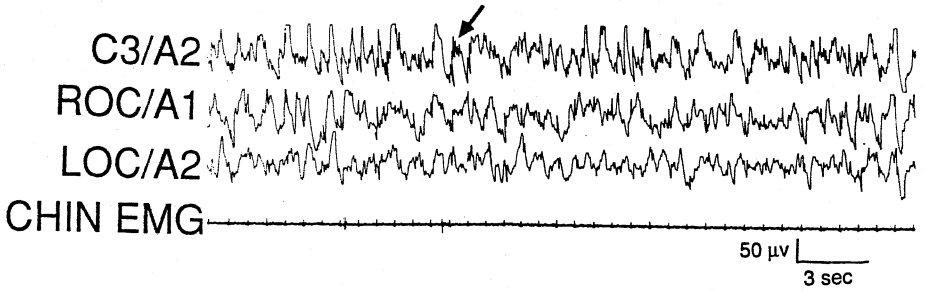

Figure 100–9. Stage 3 sleep is scored when the EEG pattern consists of high-voltage (≥75 μV), slow (≤2 cps) activity in 20% or more, but less than 50%, of a scoring epoch, as illustrated in this figure. Sleep spindles may occur in stage 3 sleep; the arrow indicates a spindle in this example of stage 3 sleep. Note that the EOG tracings pick up the high-voltage, slow wave activity, which can be seen in the ROC and LOC leads as in-phase deflections.

dence of specific activities in all three electrographic measures: "activated" or "desynchronized" EEG, bursts of rapid eye movements, and suppression of EMG activity (Fig. 100–11). The REM sleep EEG pattern is characterized as one of "relatively low voltage, mixed frequency."[1] An EEG pattern called sawtooth waves—because of their notched morphology—is fairly common during REM sleep,[32] particularly in proximity to eye movements, but is by no means a universal phenomenon. Thus, the presence of sawtooth activity is not required for staging REM sleep, although it may be very useful in equivocal instances. Sawtooth waves achieve the highest amplitude at the vertex[33] and, like much other REM sleep EEG activity, have a frequency in the theta range. Activity in the alpha range (usually 1 to 2 cps slower than waking alpha activity) may also be seen in the REM sleep EEG.[34]

Ponto-geniculo-occipital (PGO) spikes are a definitive feature of feline REM sleep,[35] and rhythmic hippocampal theta activity is a prominent REM feature in many primates, cats, dogs, and rodents.[36] In cats, PGO spikes occur singly in the transition to REM sleep and in bursts during REM sleep, usually leading other REM sleep phasic events. The scalp EEG routinely recorded in human beings is not clearly related to these characteristic REM sleep patterns of other species. Hodes and Dement,[37] however, suggested that K complexes in human beings may be an analog of the pre-REM PGO spikes because both pre-REM events are similarly associated with EMG and reflex suppression. Depth EEG recordings in human beings have also suggested the presence of PGO spikes in REM sleep.[38]

The EOG reveals bursts of rapid eye movements at intervals during REM sleep (see Fig. 100–11). The acronym REM originated with these eye movements, of course, although the term is now used to denote the full constellation of physiological events constituting this state. The density of rapid eye movement bursts within REM sleep varies with time of night; thus, earlier REM episodes contain fewer rapid eye movements than do later REM episodes.[39] The episodic nature of this sign of REM sleep often requires the sleep record scorer to scan the chart in advance of the epoch currently under scrutiny. The criteria of the standard manual[1] provide contingencies for such contextual decisions, as will be described below.

For an epoch to be considered REM sleep, in addition to the activated EEG and REM bursts, an EMG recorded in the manner described previously must obtain its lowest value. A universal feature of REM sleep in the intact organism is the tonic suppression of skeletal muscle tone and reflexes via a circuit that involves pontine activation of medullary inhibitory centers and culminates in postsynaptic hyperpolarization of brainstem and spinal motoneurons.[40] Superimposed on this background of tonic motor inhibition can be seen occasional twitches of distal muscles. In household pets, for example, paws, face, and whiskers show twitches in REM sleep. In human polysomnographic recordings, twitches appear as very short-lived EMG elevations, usually in proximity to eye movement bursts (see Fig. 100–11). Prolonged EMG elevation (15 sec or longer) in REM sleep, even in the absence of an EEG change, requires a stage shift (Fig. 100–12). Brief EMG elevations associated with an alteration in EEG or EOG activity (i.e., movement arousal) may signal a stage

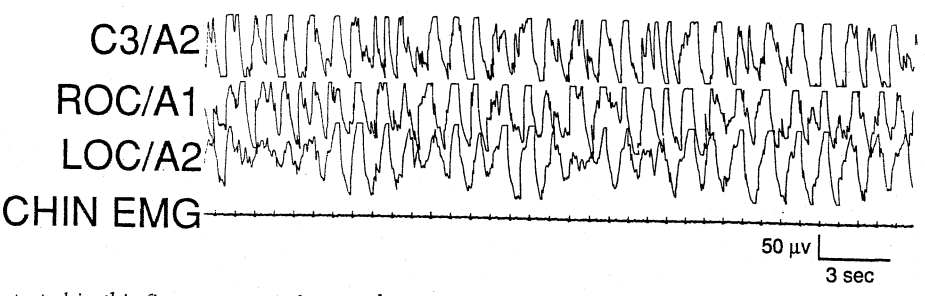

Figure 100–10. As illustrated in this figure, stage 4 sleep is characterized by a predominance (less than 50%) of high-voltage slow waves in the EEG. In this sample tracing, the slow wave EEG amplitude is so great that the pen-swing limitation of the recorder is exceeded and pen "blocking" distorts the wave shapes.

change, depending on the relative size of this movement and duration of the EEG and EOG alterations.

Both REM sleep and NREM stage 2 sleep require the presence of episodic events: bursts of rapid eye movements in REM sleep and spindles or K complexes in stage 2. In both, the background EEG is similar, that is, relatively low voltage, mixed frequency. Scoring transitions from stage 2 to REM sleep (Fig. 100–13) and from REM level to stage 2, as well as stage 2 interruptions of REM sleep (Fig. 100–14), is therefore sometimes problematic. Two fundamental guidelines in the standard manual[1]—listed below—enable one to deal with virtually every contingency.

1. Any section of record contiguous with stage REM sleep in which the EEG shows relatively low voltage and mixed frequency is scored stage REM sleep regardless of whether rapid eye movements are present, providing EMG is at the stage REM level and there are no intervening movement arousals.
2. An interval of relatively low-voltage, mixed-frequency EEG record between two sleep spindles or K complexes is considered stage 2 regardless of EMG level, if there are no rapid eye movements or movement arousals during this interval and if the interval is less than 3 min long.

The manual provides a variety of specific examples that apply these guidelines, and the reader is urged to review them.

Movement Time. Gross postural readjustments are fairly common during sleep, often occurring in the vicinity of REM episodes.[4] When such movements arise from sleep, immediately precede sleep, and obscure the EEG activity (and usually the EOG as well) for at least one half the scoring epoch, that epoch is designated "movement time." If this pattern is preceded or followed by wakefulness, it is scored as an awake pattern.

Considerations for Staging Sleep in Pathologies

The standard manual was developed to provide guidelines for staging sleep in normal adult human beings, and its recommendations are suitable for many pathologies as well. Nevertheless, full characterization of sleep in a number of sleep-related pathologies at times requires one to depart from the standard procedures. The following material briefly reviews certain issues that may arise in specific disorders and suggests alternatives for addressing these issues.

Narcolepsy. The sleep of patients with narcolepsy is characterized by sleep onset REM episodes (the occurrence of rapid eye movements within 15 min of sleep onset), mixtures of stage 2 and REM sleep, and numerous arousals relative to normal persons.[41] Each of these phenomena can be characterized using the guidelines of the standard manual. Particular care is often required, however, and one may wish to use additional procedures, such as adding a vertical EOG, to assist in identifying a brief, early REM episode. An early REM episode may not last sufficiently long to characterize a full epoch (e.g., longer than 15 sec) as REM sleep; its occurrence may nonetheless be diagnostically relevant and must be noted.

The most problematic area with narcolepsy generally involves patients who are medicated with tricyclic antidepressants. Tricyclics are commonly noted to have an REM-suppressant effect[42]; however, a REM-like state—characterized by an elevated EMG in the presence of an activated EEG and phasic rapid eye movements—occurs with a periodicity similar to that of REM sleep.[43] One might characterize this as an "anomalous" state, as shown in Table 100–3. Thus, epochs of anomalous sleep may be accounted for outside the standard criteria and staged as neither REM nor NREM sleep.[44]

Sleep Apnea Syndromes. Patients with sleep apnea syndromes experience a great increase in the frequency of arousals from sleep and in the number of body movements. Both types of activity have an impact on sleep staging. For example, a patient may be clearly asleep and apneic for 10 sec, and movement associated with the termination of the apnea may obscure the remainder of the epoch (Fig. 100–15). Another common occurrence in patients with sleep apnea syndromes is the appearance of K complexes almost exclusively at the termination of apneas. If scored exclusively using the standard guidelines, sleep might never be found in such patients or might appear as only stage 1 and movement time. The following suggestions (modified from Flagg and Coburn[45]) for scoring sleep in such patients attempt to account for these pathological events.

1. Follow standard guidelines for entry into stage 1 from wakefulness and stage 2 from stage 1. (Coding "microsleep" episodes [less than half the epoch with stage 1 EEG] at the onset of sleep may be useful.)
2. Once stage 2 sleep is scored, continue stage 2 through any arousal that does not result in a transition to wakefulness (more than half the epoch with waking EEG). (Coding "transient arousals" [see below] may be useful.)
3. In REM sleep, ignore EMG elevations that are clearly associated with snoring.
4. In adults, stages 3 and 4 may be combined. (Some investigators[45] recommend combining stages 2, 3, and 4 in patients with sleep apnea. Such crude categorization may obscure clinically relevant information and is not recommended, particularly for children.)

Alpha-Delta Sleep. An EEG pattern of alpha intrusion into NREM sleep was first noted in patients with psychiatric disorders.[46] The pattern was described as "a mixture of 5–20 per cent delta waves (more than 75 μV, 0.5–2 cps) combined with relatively large amplitude, alpha-like rhythms (7–10 cps). These alpha rhythms are usually 1–2 cps slower than waking alpha." A similar pattern has been related to a complaint of "nonrestorative" sleep in patients with musculoskeletal pain or fibrositis.[47] This EEG pattern might legitimately be scored as NREM stage 1 or 2, but the

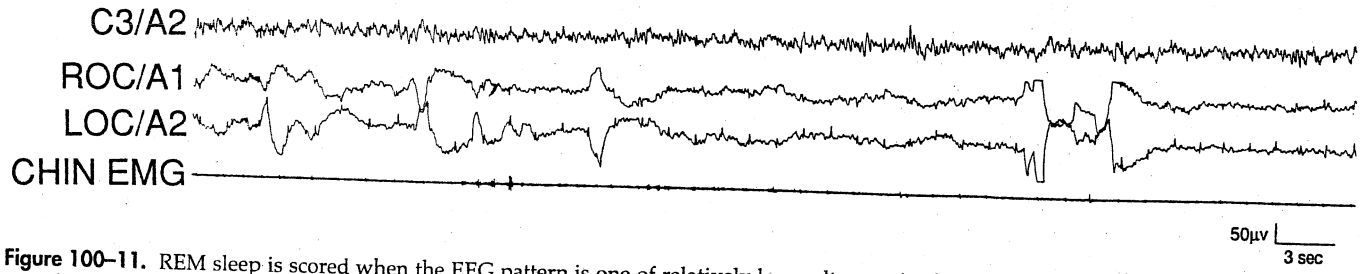

Figure 100–11. REM sleep is scored when the EEG pattern is one of relatively low voltage, mixed frequency; the EMG is tonically suppressed; and the EOG shows rapid eye movements. Each of these REM sleep components is present in this figure. The early and late portions of the figure, in which eye movement bursts occur along with EMG twitches in the earlier portion, might be characterized as "phasic" REM sleep, whereas the intervening segment containing no eye movements might be called "tonic" REM sleep. Note that eye movements appear as out-of-phase deflections in the ROC and LOC tracings.

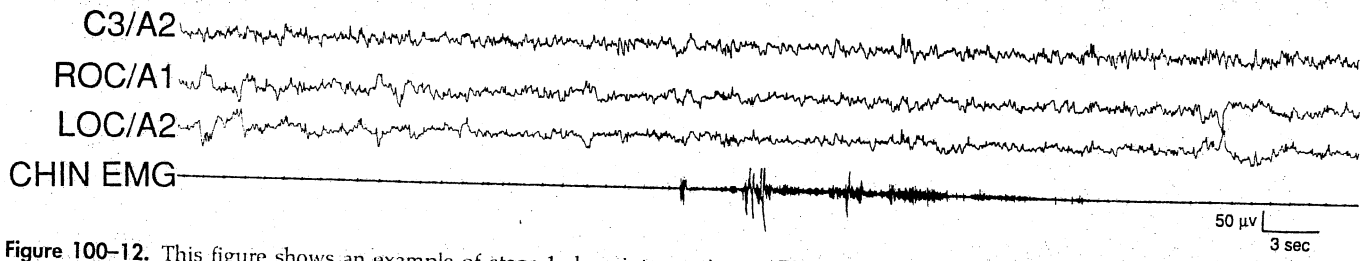

Figure 100–12. This figure shows an example of stage 1 sleep interrupting an REM episode. The interruption is seen as a tonic increase in EMG activity lasting longer than 50% of the scoring epoch. This change is scored even if the EEG pattern shows no discernible difference and even if no slow eye movements occur.

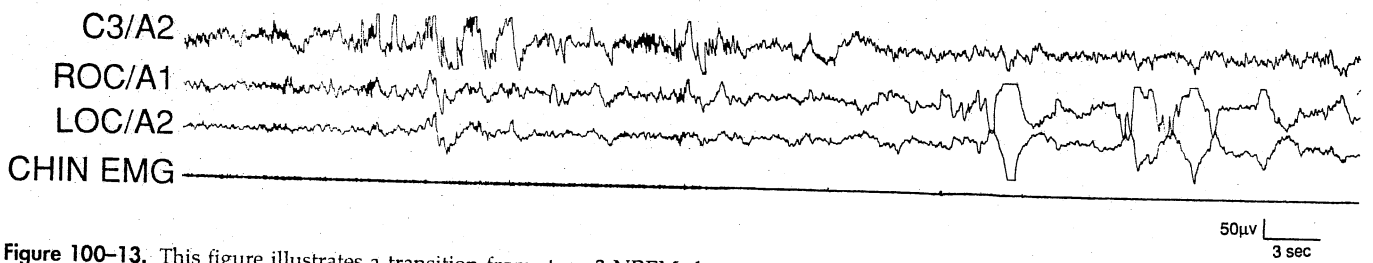

Figure 100–13. This figure illustrates a transition from stage 2 NREM sleep to REM sleep, in which the three markers of REM sleep occur in fairly close proximity. EMG suppression leads the EEG desynchronization by a few seconds, and bursts of rapid eye movements occur several seconds later. It is not uncommon for several minutes to elapse during such a transition.

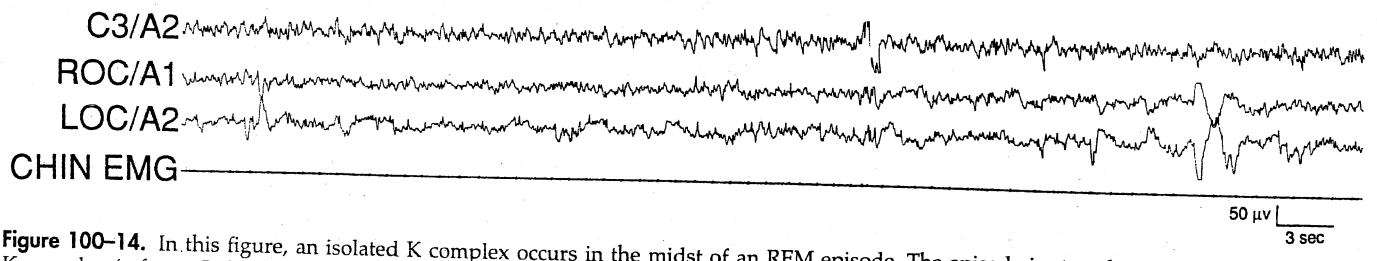

Figure 100–14. In this figure, an isolated K complex occurs in the midst of an REM episode. The episode is staged as REM sleep despite the K complex (refer to Rule 1). Had a second K complex or sleep spindle occurred, spanning more than 50% of the scoring epoch, the interval would be staged as stage 2 sleep, even if the background EEG resembled the REM pattern and the EMG were at the REM sleep level.

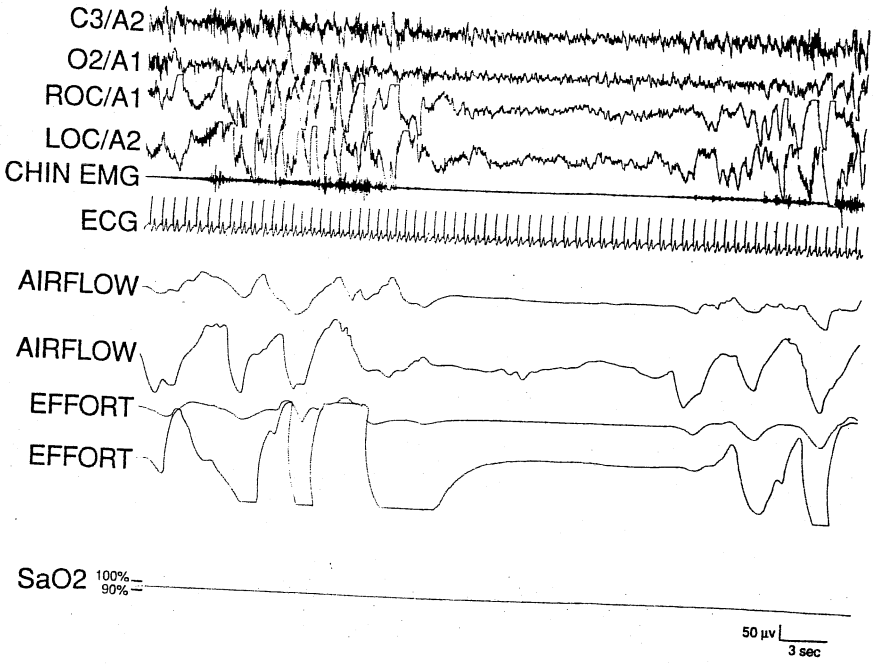

Figure 100–15. Sleep onset is aborted by a large movement associated with the termination of an episode of sleep apnea. Note that the "scorable" portion of this epoch contains only about 12 sec of stage 1 sleep, which is insufficient to characterize the entire 30-sec epoch. For this type of occurrence, the coding of a microsleep event might be useful, along with the coding of an apneic event.

clinical implications of this type of "sleep" require that it be noted and remarked on. Thus, one might define a separate sleep "stage" or use an "event" code to make this pattern accessible for separate analysis.

Transient Arousals. Many sleep disorders involve frequent, brief arousals that do not alter sleep stage scoring but that may be clinically relevant. Such arousals are a common feature of normal aging as well. Clinical implications of these brief arousals have been shown in several types of study. For example, brief arousals induced experimentally into the sleep of normal volunteers resulted in daytime sleepiness, even though the total amount of sleep was unchanged.[48] In addition, spontaneously occurring transient arousals in elderly subjects have been correlated with waking alertness level.[49] This type of arousal occurs frequently in patients with sleep apnea syndromes, periodic movements in sleep, and other sleep disorders. Therefore, cataloguing such events may be relevant in several clinical and nonclinical populations. The following definition has been proposed for transient arousals[49]: "any clearly visible EEG arousal (usually alpha rhythm) lasting two seconds or longer, but not associated with any stage or state change in the epoch scoring. These brief arousals are sometimes, but not always, associated with a body movement or respiration event." To this definition we add the recommendation that transient arousals in REM sleep be coded only when EEG alpha activity is associated with another sign of arousal (e.g., increased heart rate, EMG elevation, or respiration irregularity) because alpha activity is a fairly common feature of REM sleep.[34] A task force of the American Sleep Disorders Association (ASDA) has defined a set of scoring rules and has provided examples for coding EEG arousals during sleep.[50]

The ASDA coding system has initiated a renewed interest in sleep-related arousals, an aspect of sleep staging that has beleaguered sleep researchers and clinicians for decades. For example, a 1999 task force of the American Academy of Sleep Medicine focused on the role of repiratory-effort related arousal events in helping define the severity of the obstructive sleep apnea-hypopnea syndrome[50a] (see Chapters 79 and 101). Furthermore, as more investigators examine sleep in newly described sleep disorders and other medical disorders, this interest in sleep fragmentation strengthens. For example, the description of upper airway resistance syndrome (UARS)[51] rekindled interest in EEG arousals because the respiratory signs of UARS are less obvious than those in frank obstructive sleep apnea syndrome (OSAS) and only subtle indicators may be available.[52] In addition, the ASDA arousal staging system and related research have stimulated an examination or reexamination of arousals in other disorders such as allergic rhinitis,[53, 54] juvenile rheumatoid arthritis,[55] and Parkinson's disease.[56]

Others have begun to examine variations of the ASDA arousal scoring schema, and still others suggest that non-EEG markers may be important and even more reliable signs of arousal than the EEG. Pitson and Stradling,[57] for example, note that transient changes in blood pressure may signify arousals more reliably than cortical EEG, although Lofaso et al.[58] indicate that autonomic changes are highly correlated with the extent of EEG arousals. Less well studied is the possibility that certain sleep fragmenting phenomena are associated with subcortical events not visible in the cortical EEG signal. One suspects that such may be the case in sleep studies of children who manifest few cortical arousals even with prominent OSAS.

Automatic Sleep Stagers

Although many groups in the United States continue to analyze sleep data using human hand scoring of

polysomnographic or digitally acquired tracings, several systems for automatically staging sleep have been proposed, and a number are commercially available.[59-66] Certain of these systems are based on the standard guidelines, although several approaches that confront the sleep staging issues more from the perspective of available technologies have also been used. Thus, instead of adapting digital computer technology to human eyeball scoring criteria, they use such techniques as frequency spectra analysis or multidimensional scaling,[59] adaptive segmentation and fuzzy subset theory,[60] or expert systems approaches.[61] No single automated stager has yet emerged as the ideal alternative to hand scoring, and space does not permit a review of available systems. The following questions are offered as a basis for evaluating automatic sleep staging systems (see Chapter 110):

1. Has the system been validated against another known assessment technique?
2. Is the system valid for the types of studies for which it will be used—for example, sleep only, sleep and breathing, sleep and movements, and so forth?
3. Is the system valid for the types of patients in whom it will be used—for example, sleep apneics versus narcoleptics, medicated versus nonmedicated patients, and so on?
4. Is the system valid for the age groups in whom it will be used—children versus adults versus the elderly?
5. Is the system compatible with available laboratory hardware?
6. Does the system require excessive operator input (e.g., knob turning, "tweaking," fine tuning) that takes time equivalent to hand scoring?
7. Does the system provide output verification? That is, can the raw data be reviewed?
8. If the system does not automatically assess relevant events, can hand-scored events be accurately correlated to the stager's output?
9. Is the system sufficiently flexible to support future forseeable applications? Such applications might include changes in patient population, recording equipment, research orientation, and so forth.
10. Is the system supported by accessible consultants?

SUMMARIZING SLEEP STAGE DATA

After the sleep data are scored, they must be summarized into a comprehensible form. No consensus format has been achieved, and certain areas of controversy exist; however, a number of conventions are fairly common and include the following types of analysis. (Alternate calculation paradigms are sometimes used and have been noted where appropriate.) Figure 100–16 shows the output of one type of sleep data summary sheet.

Stages

A summary of the night will invariably include the time spent in each of the sleep stages, as well as time awake and movement time. This type of summary is relatively straightforward and noncontroversial. Calculation of percentage distributions is not quite as clear cut, as various groups may calculate sleep stage percentages based on total recording time (dark time), total sleep time (total NREM stages 1 to 4 plus REM), or sleep period time (time from sleep onset to sleep offset, including intervening arousals). The example in Figure 100–16 begs the question by using all three alternatives.

Latencies

The topic of latencies is associated with a certain amount of controversy, particularly because the type of patient may affect the appropriateness of specific definitions. Thus, although sleep latency, defined as elapsed time from lights out until the first of three consecutive epochs of stage 1 or the first of any other stage, may be appropriate for normal, noncomplaining individuals or for hypersomnolent patients, it may not be appropriate for patients with sleep onset insomnia. One alternative to the above definition requires stage 2 sleep (spindle or K complex) to define sleep onset.[65] To account for instances in which a patient may have 2 or 3 min of sleep followed by a lengthy awakening, definitions that require, for example, 5 consecutive min of sleep have been suggested by others.[66] The issue of the definition of sleep onset is nontrivial because latencies to stage 4 or REM sleep are generally calculated from sleep onset. Certain analysis programs have the capability to provide several calculations of sleep onset, whereas others provide the flexibility to redefine the criterion for individual cases. In the absence of a comprehensive database, it is not possible to make a sweeping generalization. A "safe" alternative for most clinical studies is probably to choose the conservative "5-min" rule or even a 10-min rule, although a briefer requirement might be more appropriate for patients with sleep apnea syndromes, in whom frequent awakenings may preclude such a "sleep onset" entirely.

Once a definition of sleep onset is established, determining stage 3 or 4 or REM latency is fairly straightforward: elapsed time from the (start of) defined sleep onset to the first epoch of stage 3 (or 4) or REM sleep. Certain groups may apply a "three-epoch" rule to this definition, that is, three consecutive epochs of the target stage are required. One point of dispute regarding REM latency calculation concerns whether or not to include any waking intervals that may occur between sleep onset and REM onset.[67] No firm recommendation can be made; however, it is still generally assumed that waking is included in the calculation, unless otherwise noted. Such considerations are crucial when data are compared across groups, which is particularly relevant when one uses norms from another laboratory.

T.A.

Subject's name:	T.A.
Subject's gender:	M
Subject's age:	14.0000 years
Subject's date of birth:	1/11/73
Subject's Tanner stage:	
Recording date:	1/11/87
Name of study:	T/A
Group:	
Recording condition:	PRETREATMENT
Recording technician:	CARSKADON
Scoring technician:	MANCUSO
Data entry technician:	MANCUSO

Minimum epoch length:	0.4800 minutes (Epoch 478 of Page 11)
Maximum epoch length:	0.5294 minutes (Epoch 965 of Page 10)
Average epoch length:	0.4975 minutes

	Epochs	Minutes	%TDT	%SPT	%TST
TDT	1179	586.50	-	-	-
SPT	1067	530.95	90.53	-	-
TST	1031	513.00	87.47	96.62	-
WASO	38	18.93	3.23	3.56	3.69
WAFA	82	41.00	6.99	7.72	7.99
TS1	93	46.09	7.86	8.68	8.98
TS2	546	272.43	46.45	51.31	53.11
TS3	92	45.62	7.78	8.59	8.89
TS4	167	82.91	14.14	15.61	16.16
TNREM	898	447.05	76.22	84.20	87.14
TREM	115	56.98	9.71	10.73	11.11
TSW	259	128.53	21.91	24.21	25.05
TWT	148	73.50	12.53	13.84	14.33
TMT	18	8.97	1.53	1.69	1.75

Rem Summary:

	REM1	REM2	REM3	REM4	TOTAL	MEAN
TT	3.93	8.95	21.80	27.20	61.89	15.47
REMT	2.95	8.95	21.80	23.27	56.98	14.24
S1	0.00	0.00	0.00	2.95	2.95	0.74
S2	0.98	0.00	0.00	0.00	0.98	0.25
WT	0.00	0.00	0.00	0.98	0.98	0.25
MT	0.00	0.00	0.00	0.00	0.00	0.00
SEG	2	1	1	3	7	1.75
Cycles	192.77	111.64	104.66	111.89	520.95	130.24

End of last REM from end of night: 51.00

Analysis by fraction (1/3):

	1	2	3
Wake	0.00	6.98	12.20
SW	91.94	13.18	23.41
REM	0.00	11.90	45.08

T/A, PRETREATMENT

Milestones:

Lights out:	22:14:00 (Epoch 27 of Page 1)
Sleep onset:	22:28:33 (Epoch 57 of Page 1)
Last sleep epoch:	7:19:00 (Epoch 602 of Page 13)
End of night:	8:00:30 (Epoch 685 of Page 13)

	REM	NREM	WAKE
Body movement (1)	1	43	1
Transient arousal (2)	0	4	0
Slow eye movement (4)	0	4	4
Microsleep (5)	0	0	5
Central Apnea/Hypopnea (7)	2	6	0
Obstructive Apnea/Hypopnea (A)	0	83	0
Mixed Apnea/Hypopnea (B)	0	1	0
SaO2<90% (C)	0	21	0
SaO2<80% (D)	0	0	0

Latencies (minutes):

Lights out to S1	13.58
Lights out to S2	14.55
Lights out to S3	23.50
Lights out to S4	26.00
Lights out to sleep onset	13.58
LO to 10 minutes continuous sleep	14.55
Sleep onset to slow wave	8.95
Sleep onset to REM	188.83

Figure 100–16. A sleep stage summary sheet is illustrated here. This sample represents only one of many possible summary formats. The data are taken from a night of sleep recorded in a 14-year-old boy with enlarged tonsils and adenoids who had moderately disordered breathing during sleep. The 25-min combining rule was used to define REM periods. The following definitions were used to derive specific items presented in this summary: TDT, total dark time (elapsed time from lights out to end of night); SPT, sleep period time (elapsed time from sleep onset to last epoch of sleep); TST, total sleep time; WASO, wake time after sleep onset; WAFA, wake time after final awakening; TS1 to TS4, total amount of stage 1, 2, 3, and 4 sleep; TNREM, total stages 1 + 2 + 3 + 4 sleep; TREM, total amount of REM sleep; TSW, total amount of stages 3 + 4 sleep; TWT, total amount of wakefulness; TMT, total amount of movement time. Definitions in the REM summary are as follows: TT, total time of the REM episode; REMT, amount of REM sleep; S1, S2, WT, and MT, as defined above; SEG, number of REM sleep segments within the REM period; cycles, elapsed time from sleep onset to end of first REM period, from end of first to end of second REM period, and so on. All other items are self-explanatory.

Cycles

A description of the NREM-REM cycle is a common feature of the night's sleep summary. Unfortunately, the defining characteristics for such a description are not standardized, and therefore, a number of idiosyncratic approaches have been used. One common way of defining cycles is as the elapsed time from the end of each REM episode to the end of the next REM episode, whereas another uses the time from the start of one REM episode to the start of the next. The consequences of choosing one alternative over the other have not been clearly established. Another difficulty for defining REM cycles arises from the fact that REM sleep episodes are noncontinuous–that is, as described above, REM sleep may be interrupted by stages 1 or 2, wakefulness, or movement time. Thus, one must choose a "combining rule" for defining REM episodes, which in turn defines the cycle. In the past, combining rules of 0, 5, 10, 15, and 25 min have been used.[68] (Thus, a new REM cycle is begun when the NREM interval exceeds the time designated by the combining rule.) When data are evaluated using a number of alternatives, a 15- to 25-min rule is generally recom-

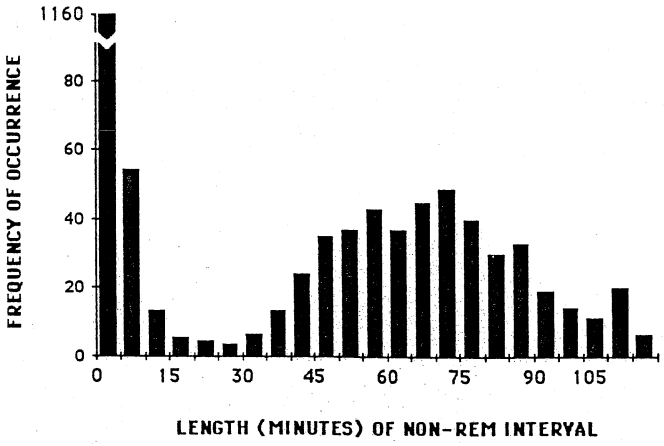

Figure 100–17. A frequency histogram illustrating the distribution of NREM (wakefulness, NREM sleep, and/or movement time) intervals of various duration during REM sleep episodes. Data are combined from the second laboratory night recorded in 82 adolescents, 18 young adults, and 26 elderly adults. Virtually no intervals of 15 to 30 min were recorded in these volunteers, suggesting that a combining rule in the range of 15 to 30 min will reflect the cyclic organization of REM sleep. (A 25-min combining rule was used in the sleep stage summary sheet in Figure 100–16.)

mended.[68] Dement[69] originally recommended a 25-min combining rule based on the frequency distribution of NREM intervals separating epochs of REM sleep. We replicated this finding, as illustrated in Figure 100–17, confirming Dement's results in adolescent, adult, and elderly volunteers. These data suggest that a combining rule of 15 to 30 min will provide the best description of REM sleep in human beings.

Partitioning the Night

For many years, it has been a common practice to examine at least waking, slow-wave (stages 3 + 4) sleep, and REM sleep by thirds of the night. This practice, at least for REM sleep, seems to have originated in early studies of insomnia and sleeping pills.[70] Its usefulness derives primarily from normative studies in young adults, in which one sees a predominance of stage 3 and 4 NREM sleep in the first third of sleep and a predominance of REM sleep toward the last third of sleep. In insomniacs, preferential distribution of waking to a third of the night may provide insight regarding the type of sleep problem.[71] Although these specific comparisons are not always useful or appropriate, the "thirds of night" analysis remains a valuable thumbnail description of a night's sleep. Other variations of this partitioning technique may use halves or quarters of the night or even hour-by-hour assessment (Fig. 100–18).

Events

Events coded during sleep (see Table 100–2) are frequently tabulated according to whether they occurred in NREM or REM sleep. Finer distinctions are rarely made. When the event spans more than one epoch (e.g., respiratory disturbance), it is recommended that it be catalogued according to the stage in which it began.

Analysis by fraction (1/3):

	1	2	3
Wake	0.00	6.98	12.20
SW	91.94	13.18	23.41
REM	0.00	11.90	45.08

Analysis by fraction (1/4):

	1	2	3	4
Wake	0.00	1.00	8.45	9.72
SW	79.29	12.65	19.48	17.11
REM	0.00	2.95	20.09	33.93

Analysis by fraction (1/2):

	1	2
Wake	1.00	18.18
SW	91.94	36.59
REM	2.95	54.03

Analysis by interval (60 minutes):

	1	2	3	4	5	6	7	8	9
Wake	0.00	0.00	0.00	0.00	5.50	1.48	3.47	0.00	17.53
SW	43.82	22.67	25.45	0.00	0.00	17.50	1.98	13.19	3.91
REM	0.00	0.00	0.00	2.95	4.55	4.41	21.80	0.00	23.27

Figure 100–18. The sleep data summary may partition the night in one of several ways, depending on the purpose of the study or the questions being asked. The example in this figure, based on the night summarized in Figure 100–16, illustrates partitioning by thirds, quarters, and halves of the night and hour-by-hour across the night.

Sleep Histogram

Another way to examine events is in correlation with the ongoing pattern of nocturnal sleep, as visualized using histogram plotting techniques. Figure 100–19 shows an example of such a plot. Sleep stages and transitions are illustrated in the upper portion of the plot and show the unfolding of sleep versus time. This type of graphic display has been used from the earliest modern sleep studies.[4] Events are usually plotted below the histogram, aligned temporally with their occurrence. This plotting technique provides a sometimes very helpful visual representation of the data, and many software packages that provide data reduction of sleep stages and events also have such plotting capabilities.

WHY STAGE SLEEP?

A number of investigators and clinicians coming to the field of sleep from other disciplines question the necessity for evaluating sleep stages, particularly in clinical conditions. Thus, for example, a pulmonary specialist may question sleep staging in a patient with apnea for whom the key issues to the specialist may be length of apnea, degree of desaturation, cardiac arrhythmias, and so forth. A urologist's focus may be penile circumference, which does not require distinctions of sleep staging. Thus, an argument can be and has been made for focusing on the pathological event rather than sleep per se. A few counterarguments are offered below.

Regulatory Physiology Differs From Waking to NREM to REM Sleep

As increasing numbers of systems are evaluated during naturally occurring wakefulness and sleep, it has become quite clear that many regulatory mechanisms are affected by state.[72] For example, the ventilatory responses to oxygen and carbon dioxide (see Chapter 16) are somewhat damped in NREM sleep and may be absent in REM sleep.[73, 74] Another dramatic example concerns thermoregulation. Thermoregulatory responses are only slightly altered in NREM sleep and virtually totally lacking in REM sleep.[75] Such marked state-dependent alterations in regulatory physiology must be taken into account to assess fully the implications of observed sleep-related pathologies.

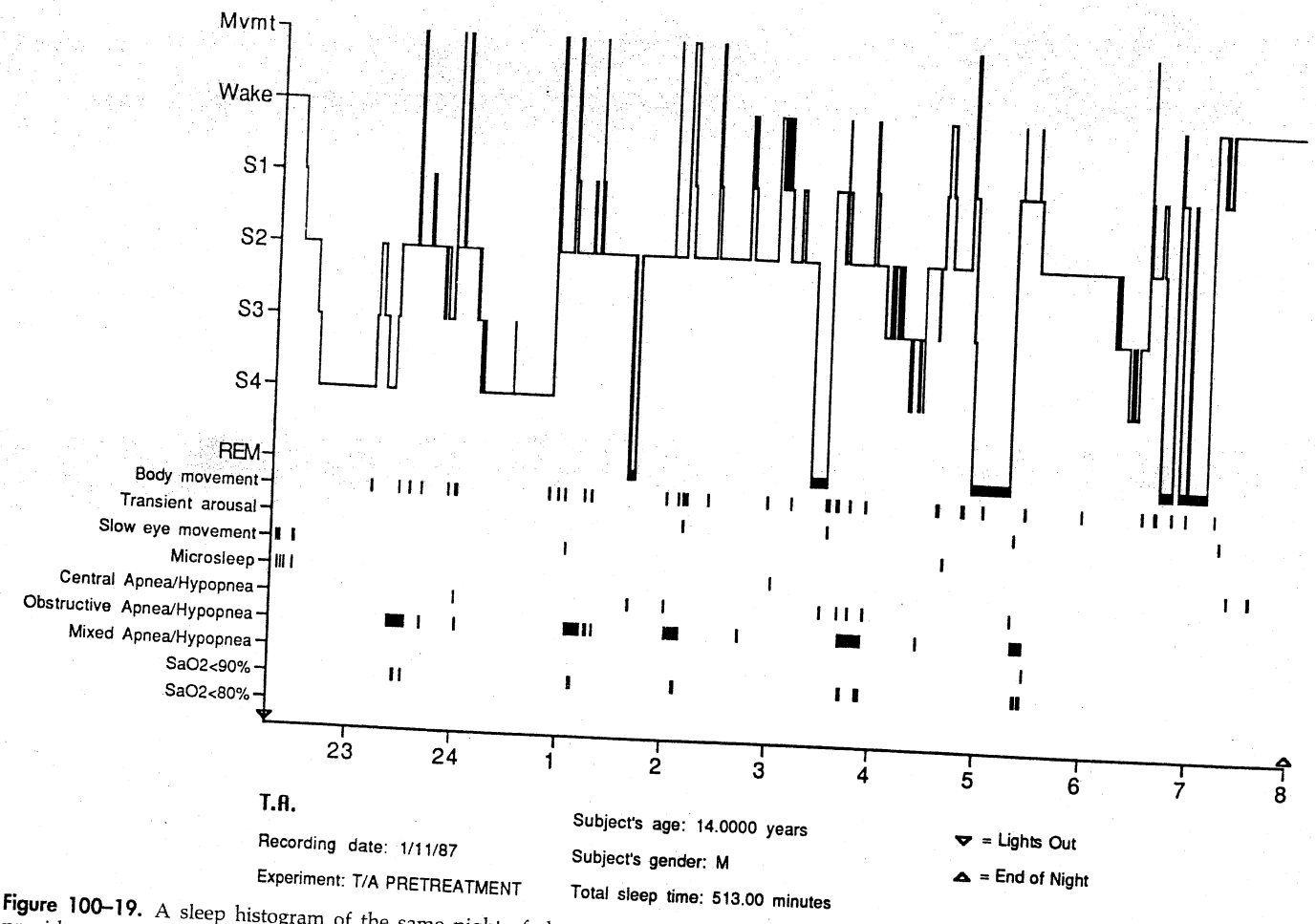

Figure 100–19. A sleep histogram of the same night of sleep summarized in Figure 100–16 is shown in this figure. The sleep histogram provides a graphic display of the night using an analog plot of sleep-wake stages across time *(upper portion)*. Arrayed beneath this plot are event markers, which are temporally aligned.

Pathological Events Disturb Sleep

Patients with sleep apnea syndromes, for example, have markedly disrupted sleep. In children, the disruption may preferentially reduce stage 3 and 4 sleep,[76] and sleep apnea may be associated with growth problems[77]; in adults, sleep apnea is more likely to occur during, and be disruptive of, REM sleep.[78] The possible clinical relevance of such a sleep disturbance in a child is obvious but cannot be appreciated if sleep states are not evaluated. Documentation of recovery sleep following treatment may also provide insights into therapeutic efficacy that may be unrelated to the pathological events (apneas) per se.

Arousals consequent to sleep pathologies are also clinically relevant and require assessment to fully characterize the pathology. Thus, as mentioned previously, arousals are clearly related to daytime sleepiness.[48, 49] In the case of sleep apnea syndromes, a given treatment may improve the apnea–as documented by maintenance of Sa_{O_2} at more than 85%, reduction in cardiac arrhythmias, and conversion of apneas to hypopneas–yet the patient may still suffer arousals from sleep sufficient to impair waking function or to be associated with a vulnerability to unintentional sleep episodes. Hence, it is relevant to evaluate sleep and arousals, as well as the respiratory function in such patients. Arousals may be a relevant issue in the case of periodic movements during sleep, as well. One study has documented clinical improvement of patients in whom periodic movements during sleep were treated with benzodiazepine hypnotics, although the number of movements was unchanged from pretreatment.[79] The number of associated arousals and the amount of transitional stage 1 sleep were reduced, however, a factor that would have been overlooked had sleep staging not been performed.

Sleep State May Affect Pathology

It has been known for many years that penile tumescence occurs in association with REM sleep in normal males of virtually all ages.[80] This phenomenon has been capitalized on to assess erectile dysfunction by recording REM sleep–related nocturnal penile tumescence (NPT).[81] Various clinicians, however, have attempted to perform studies of NPT in patients outside the sleep laboratory using such techniques as the "postage stamp method."[82] Other methodological considerations aside[83] (because the argument obtains even if appropriate NPT techniques are used without monitoring sleep stage), one cannot achieve a valid test of NPT if sleep is not assessed. This is true simply because an "abnormal" NPT can result if REM sleep is abnormal, disrupted, or absent. Sleep disorders themselves may have an impact on NPT as well.[84] Therefore, without evaluating sleep, it is not possible to determine whether tumescence did not occur because erectile function was impaired or sleep was disturbed.

Another example again concerns sleep apnea syndromes. As mentioned previously, sleep apneas in a percentage of adult patients may occur preferentially in REM sleep.[78] It has been suggested that diagnostic assessment of sleep apneas can be performed by monitoring respiration during a daytime nap.[85] In this case, in particular, sleep monitoring is essential because REM sleep may not occur during a daytime nap (depending on the time of the nap[86]), and therefore, the severity of sleep apnea may be very greatly underestimated. Without documentation of sleep state, such important clinical judgments (including optimal continuous positive airway pressure) may not be possible.[86a]

An Abnormal Sleep Architecture May Be a Marker of Pathology

Patients with narcolepsy often enter sleep through REM sleep, rather than experiencing the normal transition from waking to NREM sleep.[41, 87] Because the symptom presentation of narcolepsy is variable,[88] it is relevant to document the sleep onset transition in patients with complaints of hypersomnolence. Relatively short REM onset latencies are also thought to be a marker of endogenous depression.[89]

In summary, laboratory monitoring and staging of sleep remain important components in the assessment of patients with sleep disorders. The techniques derive directly from the earliest studies following the discovery of REM sleep in the 1950s, and some might criticize that the procedures have not kept pace with technological advances. Because automated, ambulant systems that are inexpensive, validated, and reliable are marketed, it is likely that polysomnography will advance accordingly.

The Newborn Infant

Because of rapid changes in the nervous system after birth, the well-defined *stages* seen in the adult are not present, and special criteria are used to define *states*. The standard scoring manual for neonates[16] defines sleep states using behaviors, respiration, eye movements, the EEG, and muscle tone. The following states were defined: active-REM sleep, quiet sleep, and indeterminate sleep. Criteria for defining these states with examples of sleep recordings in neonates are found in the standard scoring manual for neonates.[16]

Acknowledgments

We thank Lisa Donovan for typing the manuscript, Joan Mancuso for assembling the figures, and Sharon Keenan, REEGT, RPSGT, for her comments on the technical accuracy of the manuscript.

References

1. 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.
2. Loomis AL, Harvey EN, Hobart GA. Electrical potentials of the human brain. J Exp Psychol. 1936;19:249–279.

3. Aserinsky E, Kleitman N. Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. Science. 1953;118:273–274.
4. Dement WC, Kleitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. Electroencephalogr Clin Neurophysiol. 1957;9:673–690.
5. Berger RJ. Tonus of extrinsic laryngeal muscles during sleep and dreaming. Science. 1961;134:840.
6. Jouvet M, Michel M. Correlations electromyographiques du sommeil chez le chat décortique et mesencephalique chronique. CR Soc Biol (Paris). 1959;153:422–425.
7. Jasper HH (Committee Chairman). The ten twenty electrode system of the International Federation. Electroencephalogr Clin Neurophysiol. 1958;10:371–375.
8. Grass ER. A Second AIDS Alert. Quincy, Mass: Grass Instrument Company Bulletin; September 1–2, 1985.
9. Blake H, Gerard RW, Kleitman N. Factors influencing brain potentials during sleep. J Neurophysiol. 1939;2:48–60.
10. Brazier MAB. The electrical fields at the surface of the head during sleep. Electroencephalogr Clin Neurophysiol. 1949;1:195–204.
11. Carskadon MA. Basics for polygraphic monitoring of sleep. In: Guilleminault C, ed. Sleeping and Waking Disorders: Indications and Techniques. Menlo Park, Calif: Addison-Wesley: 1982:1–16.
12. Williams RL, Karacan I, Hursch CJ. EEG of Human Sleep: Clinical Applications. New York, NY: John Wiley & Sons; 1974.
13. Carskadon MA. The second decade. In: Guilleminault C, ed: Sleeping and Waking Disorders: Indications and Techniques. Menlo Park, Calif: Addison-Wesley; 1982:99–125.
14. Coble PA, Kupfer DJ, Taska LS, et al. EEG sleep of normal healthy children, part I: findings using standard measurement methods. Sleep. 1984;7:289–303.
15. Carskadon MA, Orav EJ, Dement WC. Evolution of sleep and daytime sleepiness in adolescents. In: Guilleminault C, Lugaresi E, eds. Sleep/Wake Disorders: Natural History, Epidemiology, and Long-Term Evolution. New York, NY: Raven Press; 1983:201–216.
16. Anders T, Emde R, Parmelee A, eds. A Manual of Standardized Terminology: Techniques and Criteria for Scoring of States of Sleep and Wakefulness in Newborn Infants. Los Angeles, Calif: UCLA Brain Information Service/Brain Research Institute; 1971.
17. Guilleminault C, Souquet M. Sleep states and related pathology. In: Korobkin R, Guilleminault C, eds. Advances in Perinatal Neurology. New York, NY: Spectrum; 1979:225–247.
18. Carskadon MA. Determinants of daytime sleepiness: adolescent development, extended and restricted nocturnal sleep [dissertation]. Stanford, Calif: Stanford University; 1979.
19. DiPerri R, Meduri M, DiRosa AE, et al. Sleep spindles in healthy people, I: quantitative, automatic analysis in young-adult subjects. Boll Soc Ital Biol Sper. 1977;53:983–989.
20. Dement WC. The nature and function of sleep. In: Reynolds D, Sjoberg A, eds. Neuroelectric Research: Electroneuroprosthesis, Electroanesthesia, and Nonconvulsive Electrotherapy. Springfield, Ill: Charles C Thomas; 1970:171–204.
21. Gaillard J-M, Blois R. Spindle density in sleep of normal subjects. Sleep. 1981;4:385–391.
22. Johnson LC, Spinweber CL, Seidel WF, et al. Sleep spindle and delta changes during chronic use of a short-acting and a long-acting benzodiazepine hypnotic. Electroencephalogr Clin Neurophysiol. 1983;55:662–667.
23. Crowell DH, Kapuniai LE, Boychuk RB, et al. Daytime sleep stage organization in three-month-old infants. Electroencephalogr Clin Neurophysiol. 1982;53:36–47.
24. Ellingson RJ. Development of sleep spindle bursts during the first year of life. Sleep. 1982;5:39–46.
25. Shibagaki M, Kiyono S, Watanabe K. Spindle evolution in normal and mentally retarded children: a review. Sleep. 1982;5:47–57.
26. Prinz PN, Raskind M. Aging and sleep disorders. In: Williams R, Karacan I, eds. Sleep Disorders: Diagnosis and Treatment. New York, NY: John Wiley & Sons; 1978:303–321.
27. Principe JC, Smith JR. Sleep spindle characteristics as a function of age. Sleep. 1982;5:73–84.
28. Hirschkowitz M, Thornby JI, Karacan I. Sleep spindles: pharmacologic effects in humans. Sleep. 1982;5:85–94.
29. Van Leeuwen S (chairman). Proposal for an EEG terminology by the Terminology Committee of the International Federation for Electroencephalography and Clinical Neurophysiology. Electroencephalogr Clin Neurophysiol. 1966;20:293–304.
30. Johnson LC, Karpan WE. Autonomic correlates of the spontaneous K complex. Psychophysiology. 1968;4:444–452.
31. Halász P, Pál I, Rajna P. K complex formation of the EEG in sleep: a survey and new examinations. Acta Physiol Acad Sci Hung 1985;65:3–35.
32. Berger RJ, Olley P, Oswald I. The EEG, eye movements and dreams of the blind. Q J Exp Psychol. 1962;14:182–186.
33. Yasoshima A, Hayashi H, Iijima S, et al. Potential distribution of vertex sharp wave and saw-toothed wave on the scalp. Electroencephalogr Clin Neurophysiol. 1984;58:73–76.
34. Johnson LC, Nute C, Austin MT, et al. Spectral analysis of the EEG during waking and sleeping. Electroencephalogr Clin Neurophysiol. 1967;23:80.
35. Jouvet M. Neurophysiology of the states of sleep. Physiol Rev. 1967;47:117–177.
36. Freemon FR. Sleep Research: A Critical Review. Springfield, Ill: Charles C Thomas; 1972.
37. Hodes R, Dement WC. Depression of electrically induced reflexes ("H-reflexes") in man during low voltage EEG "sleep." Electroencephalogr Clin Neurophysiol. 1964;17:617–629.
38. Salzarulo P, Lairy GC, Bancaud J, et al. Direct depth recording of the striate cortex during REM sleep in man: are there PGO potentials? Electroencephalogr Clin Neurophysiol. 1975;38:192–202.
39. Aserinsky E. The maximal capacity for sleep: rapid eye movement density as an index of sleep satiety. Biol Psychiatry. 1969;1:147–159.
40. Chase MH. Synaptic mechanisms and circuitry involved in motoneuron control during sleep. Int Rev Neurobiol. 1983;24:213–258.
41. Montplaisir J, Billiard M, Takahashi S, et al. Twenty-four-hour recording in REM-narcoleptics with special reference to nocturnal sleep disruption. Biol Psychiatry 1978;13:73–89.
42. Passouant P, Cadilhac J, Ribstein M. Les privations de sommeil avec mouvements oculaires par les antidépresseurs. Rev Neurol. 1972;127:173–192.
43. Passouant P, Cadilhac J, Billiard M, et al. La suppression du sommeil paradoxal par la clomipramine. Thérapie. 1973;28:379–392.
44. Raynal DM. Polygraphic aspects of narcolepsy. In: Guilleminault C, ed. Narcolepsy. New York, NY: Spectrum, 1976:669–684.
45. Flagg WH, Coburn SC. Appendix 2: polygraphic aspects of sleep apnea. In: Guilleminault C, Dement WC, eds. Sleep Apnea Syndromes. New York, NY: Alan R Liss, 1978:357–363.
46. Hauri P, Hawkins DR. Alpha-delta sleep. Electroencephalogr Clin Neurophysiol. 1973;34:233–237.
47. Moldofsky H, Scarisbrick P, England R, et al. Musculoskeletal symptoms and nonREM sleep disturbance in patients with "fibrositis syndrome" and healthy subjects. Psychosom Med. 1975;37:341–351.
48. Stepanski E, Salava W, Lamphere J, et al. Experimental sleep fragmentation and sleepiness in normal subjects: a preliminary report. Sleep Res. 1984;13:193.
49. Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: relationship to daytime sleep tendency. Neurobiol Aging. 1982;3:321–327.
50. Guilleminault C. EEG arousals: scoring rules and examples. Sleep. 1992;15:173–184.

50a. American Academy of Sleep Medicine. Sleep related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Sleep. 1999;22:667–689.

51. Exar EN, Collop NA. The upper airway resistance syndrome. Chest. 1999;115:1127–1139.
52. Hosselet JJ, Norman RG, Ayappa I, et al. Detection of flow limitation with a nasal cannula/pressure transducer system. Am J Respir Crit Care Med. 1998;157:1461–1467.
53. Lavie P, Gertner R, Zomer J, et al. Breathing disorders in sleep associated with "microarousals" in patients with allergic rhinitis. Acta Otolaryngol. 1981;92:529–533.
54. Craig TJ, Teets S, Lehman EB, et al. Nasal congestion secondary to allergic rhinitis as a cause of sleep disturbance and daytime fatigue and the response to topical nasal corticosteroids. J Allergy Clin Immunol. 1998;101:633–637.

55. Zamir G, Press J, Tal A, et al. Sleep fragmentation in children with juvenile rheumatoid arthritis. J Rheumatol. 1998;25:1191–1197.
56. Stocchi F, Barbato L, Nordera G, et al. Sleep disorders in Parkinson's disease. J Neurol. 1998;245:S15–S18.
57. Pitson DJ, Stradling JR. Autonomic markers of arousal during sleep in patients undergoing investigation for obstructive sleep apnoea, their relationship to EEG arousals, respiratory events and subjective sleepiness. J Sleep Res. 1998;7:53–59.
58. Lofaso F, Goldenberg F, Dortho MP, et al. Arterial blood pressure response to transient arousals from NREM sleep in nonapneic snorers with sleep fragmentation. Chest. 1998;113:985–991.
59. Burger D, Cantani P, West J. Multidimensional analysis of sleep electrophysiological signals. Biol Cybern. 1977;26:131–139.
60. Gath I, Bar-on E. Computerized method for scoring of polygraphic sleep recordings. Comput Prog Biomed. 1980;11:217–223.
61. Ray SR, Lee WD, Morgan CD, et al. Computer sleep stage scoring—an expert system approach. Int J Biomed Comput. 1986;19:43–61.
62. Gaillard J-M, Tissot R. Principles of automatic analysis of sleep records with a hybrid system. Comput Biomed Res. 1973;6:1–13.
63. Smith JR, Karacan I, Lang M. Automated analysis of human sleep EEG. Waking Sleep. 1978;2:75–82.
64. Martens WLJ, Declerck AC, Kums DJThm, et al. Considerations on a computerized analysis of long-term polygraphic recordings. In: Stefan H, Burr W, eds. EEG Monitoring. Stuttgart, Germany: Gustav Fischer; 1982:265–274.
65. Agnew HW, Webb WB. Measurement of sleep onset by EEG criteria. Am J EEG Technol. 1972;12:127–134.
66. Webb WB. Recording methods and visual scoring criteria of sleep records: comments and recommendations. Percept Mot Skills. 1986;62:664–666.
67. Kupfer DJ, Targ E, Stack J. Electroencephalographic sleep in unipolar depressive subtypes: support for a biological and familial classification. J Nerv Ment Dis. 1982;170:494–498.
68. Webb WB, Dreblow LM. The REM cycle, combining rules and age. Sleep. 1982;5:372–377.
69. Dement WC. Physiology of Dreaming [dissertation]. Chicago, Ill: University of Chicago; 1958.
70. Kales A, Allen C, Scharf M, et al. Hypnotic drugs and their effectiveness: all-night EEG studies of insomniac subjects. Arch Gen Psychiatry. 1970;23:226–232.
71. Kales A, Bixler EO, Vela-Bueno A, et al. Biopsychobehavioral correlates of insomnia, III: polygraphic findings of sleep difficulty and their relationship to psychopathology. Int J Neurosci. 1984;23:43–56.
72. Orem J, Barnes CD, eds. Physiology in Sleep. New York, NY: Academic Press; 1980.
73. Phillipson EA, Sullivan CE, Read DJ, et al. Ventilatory and waking responses to hypoxia in sleeping dogs. J Appl Physiol. 1978;44:512–520.
74. Phillipson EA, Kozar LF, Rebuck AS, et al. Ventilatory and waking responses to CO_2 in sleeping dogs. Am Rev Respir Dis. 1977;115:251–259.
75. Parmeggiani PL. Temperature regulation during sleep: a study in homeostasis. In: Orem J, Barnes CD, eds. Physiology in Sleep. New York, NY: Academic Press; 1980:98–145.
76. Guilleminault C, Eldridge FL, Simmons FB, et al. Sleep apnea in eight children. Pediatrics. 1976;58:23–31.
77. Brouillette RT, Fernbach SK, Hunt CE. Obstructive sleep apnea in infants and children. J Pediatr. 1982;100:31–40.
78. Sackner MA, Lauda J, Forrest T, et al. Periodic sleep apnea: chronic sleep deprivation related to intermittent upper airway obstruction and central nervous system disturbance. Chest. 1975;67:164–171.
79. Mitler MM, Browman CP, Menn SJ, et al. Nocturnal myoclonus: treatment efficacy of clonazepam and temazepam. Sleep. 1986;9:385–392.
80. Karacan I. The developmental aspect and the effect of certain clinical conditions upon penile erection during sleep. Excerpta Med. 1966;150:2356–2359.
81. Karacan I. The clinical value of nocturnal erection in the prognosis and diagnosis of impotence. Hum Sex. 1970;4:27–34.
82. Barry JM, Blank B, Bioleau M. Nocturnal penile tumescence monitoring with stamps. Urology. 1980;15:171–172.
83. Karacan I, Aslan C, Williams RL. Reliability of stamp ring as indicator of penile rigidity in the diagnosis of impotence. Sleep Res. 1982;11:202.
84. Pressman MR, DiPhillips MA, Kendrick JI, et al. Problems in the interpretation of nocturnal penile tumescence studies: disruption of sleep by occult sleep disorders. J Urol. 1986;136:595–598.
85. Goode GB, Slyter HM. Daytime polysomnogram diagnosis of sleep apnea. Trans Am Neurol Assoc. 1980;105:367–370.
86. Karacan I, Finley W, Williams R, et al. Changes in stage 1-REM and stage 4 sleep during naps. Biol Psychiatry. 1970;2:261–265.
86a. Oksenberg A, Silverberg DS, Arons E, et al. The sleep supine position has a major effect on optimal nasal continuous positive airway pressure: relationship with rapid eye movements and non-rapid eye movements sleep, body mass index, respiratory disturbance index, and age. Chest. 1999;116:1000–1006.
87. Vogel G. Studies in the psychophysiology of dreams, III: the dreams of narcolepsy. Arch Gen Psychiatry. 1960;3:421–428.
88. Zarcone V. Narcolepsy: a review of the syndrome. N Engl J Med. 1973;288:1156–1166.
89. Kupfer DJ. A psychobiologic marker for primary depressive disease. Biol Psychiatry. 1976;11:159–174.
90. Harner PF, Sannit T. A Review of the International Ten-Twenty System of Electrode Placement. Quincy, Mass: Grass Instrument Company; 1974.