

# **Practical Guide for Clinical Neurophysiologic Testing**

*EP, LTM, IOM, PSG, and NCS*



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## ***EP, LTM, IOM, PSG, and NCS***

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# Foreword

Neurophysiologic testing has become increasingly useful in several medical specialties, including orthopedic surgery, neurosurgery, cardiology, ophthalmology, and otolaryngology, to mention only a few. But no specialty has made greater capital of measuring and analyzing the electrical properties of an organ system than neurology. The electrophysiology of the brain and spinal cord is more complex than the heart, and arguably more so than the retina or inner ear, so it should come as no surprise that neurologists have invested decades of effort to refining techniques that can objectively measure neurological function in the neurophysiology laboratory and supplement the clinical neurological examination.

In this book, Dr. Thoru Yamada, Ms. Elizabeth Meng, and their colleagues reveal what their combined extensive experience has taught them about neurophysiologic testing. There are several general points of emphasis in this book that will become very apparent to the reader. First, an understanding of the anatomy of the nervous system region being tested is critical to obtaining meaningful clinical information from neurophysiologic testing. Accordingly, an overview of the anatomy is typically found at the beginning of each chapter in this book. Second, meticulous technique is required in order to obtain results that the clinician can believe in and use to make critical clinical decisions. Such meticulous technique depends on a productive partnership between the physician and the technologist; total devotion to excellence in only one of the members of this team will not yield a satisfactory result. This is the credo that has characterized the neurophysiology laboratories at the University of Iowa since their beginning over seven decades ago under the leadership of Dr. John Knott, one of the pioneers in establishing the clinical utility of electroencephalography. These principles have also formed the core of the longstanding and successful educational program for END (ElectroNeuroDiagnostic) technologists at Iowa, one of the oldest continually functioning programs of its type in the nation. It is this same tradition of excellence that now forms the basis of practice for scores of laboratories around the world whose physicians or technologists

trained under Dr. Yamada and Ms. Meng and their colleagues at Iowa.

Recognition of the historical and current national role of Iowa neurologists and technologists has come in the form of their election to important national positions as officers of the American Society for Electrodiagnostic Technologists (ASET) (Ms. Margaret Gordon, past president) and selection as members of the American Board of Registration of Electroencephalographic and Evoked Potential Technologists (ABRET) (Dr. Thoru Yamada and Ms. Elizabeth Meng), and as current president of the ABRET (Ms. Marjorie Tucker). Dr. Yamada and Ms. Meng also served as members of the Committee on Accreditation of Electroneurodiagnostic Programs (CoA END) under the auspices of the Commission on Accreditation of Allied Health Education Program (CAAHEP). As a neurologist and clinical neurophysiologist, Dr. Yamada served as a member of American Board of Clinical Neurophysiology (ABCN), as an editorial board member of the *Journal of Clinical Neurophysiology* (official journal of the American Clinical Neurophysiology Society) and *Clinical Neurophysiology* (official journal of the International Federation of Clinical Neurophysiology), and as a medical editor for the *American Journal of Electroneurodiagnostic Technology* (official journal of the ASET).

The serious student of clinical neurophysiologic testing will find this volume to be more than a "how to" manual and a compendium of the rationale, technique, and interpretation of tests that are inherent to the modern practice of neurology. If these features are not enough to merit our praise of this volume, the pearls and pit falls of the contributors' combined decades of experience are certainly the topping on this wonderful confection of instruction.

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# Preface

When we wrote *Practical Guide for Clinical Neurophysiologic Testing: EEG* (referred to as “*Practical Guide: EEG*” in this text book), our intention was to write a comprehensive, basic text book for the END technologist as well as the neurology resident. It soon became obvious that such a text would be too cumbersome. It also seemed logical to us that the basics of EEG knowledge serve as the basis for knowledge in the other disciplines; therefore, we felt that the initial text should be EEG.

That, of course, left us with a second textbook that we now present, *Practical Guide for Clinical Neurophysiologic Testing: EP, LTM, IOM, PSG, and NCS*. With so many subspecialties represented in this text, it served the reader best to offer the writing of chapters to those who have proven expertise in each area. The University of Iowa’s Department of Neurology is blessed to have such experts either currently or recently in their employ. We have drawn from the best to present this textbook as the remainder of our quest for a comprehensive, basic END

reference. That being said, we give our sincere thanks to the chapter authors. Without them, we would not be able to offer this text. We are also indebted to Deb Stratton, as always, for her administrative skills.

This book offers the basic knowledge and technique for the END technologist and, at the same time, challenging chapters that will help the neurology resident gain insight into the patient’s condition. It is not intended to be a comprehensive review of each specialty. We have included an on-line question bank, which is intended to serve as a guide to the reader’s basic understanding of the chapter rather than as a preparation for certification/registration examinations. We hope that it will become a valuable resource for every comprehensive END laboratory.

*Thoru Yamada, MD  
Elizabeth Meng, BA, R.EEG/EP T.*

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## SECTION I

# Evoked Potentials

### CHAPTER

# 1

Thoru Yamada  
Elizabeth Meng  
Peter Seaba

## Principles of Evoked Potentials

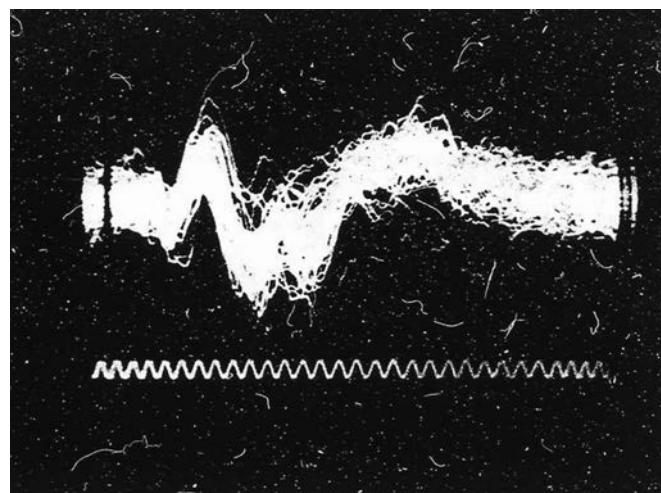
### INTRODUCTION

The evoked potential (EP) is an electrical response of the nervous system to various sensory stimuli. Unlike the EEG that shows the constantly and spontaneously changing electrical activity of the brain, the EP is time locked to the onset of the stimulation and consists of a series of waves characteristic to each stimulus modality. For clinical testing, visual, auditory, and somatosensory stimuli are used. Some EPs, such as the driving response to photic stimulation or lambda waves in response to scanning eye movements, are readily identified in routine EEG. However, most EPs have a small or a low amplitude ( $<5\text{ }\mu\text{V}$ ) and are partially or totally obscured by ongoing spontaneous EEG activity and noise. George Dawson was the first to successfully extract EP contaminated by the spontaneous EEG activity by using a photographic superimposition technique in which the sensory response to a single stimulation was repeatedly photographed and superimposed on one another (Fig. 1-1).<sup>1</sup> By this technique, he was able to demonstrate the overall EP configuration while eliminating the spontaneous activity not related to the stimulus. He later used an electronic summation technique (Fig. 1-2),<sup>2</sup> which has evolved into the computer-averaging technique currently used for clinical applications.

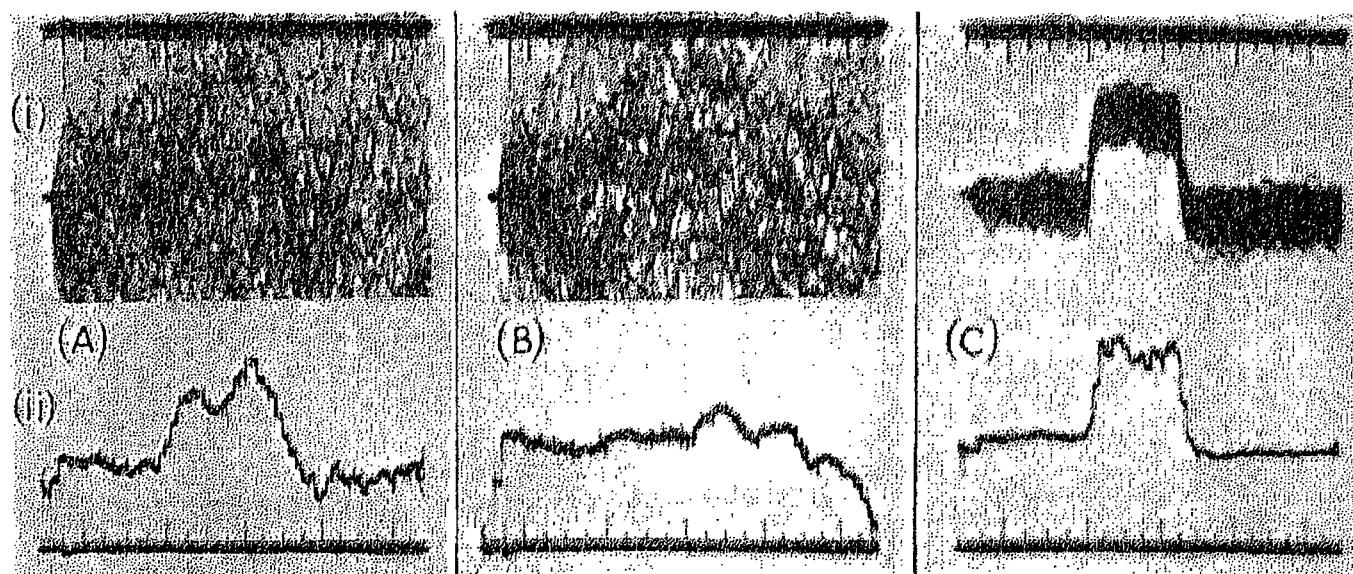
### PRINCIPLES OF AVERAGING METHOD

Although some brain responses to sensory stimulus, such as photic-induced occipital responses, are visible in a routine EEG recording (Fig. 1-3), most electric responses of the brain, brainstem, or spinal cord to a single stimulus are very small ( $<5\text{--}20\text{ }\mu\text{V}$ )

when recorded from the scalp or the body surface. They are obscured by ongoing EEG activity or contaminated by EKG, EMG, or other biological and nonbiological electrical activities. The averaging method allows extracting the response or signal (which is time locked to the stimulus) from the noise (random electrical activity unrelated to the stimulus). This is accomplished by collecting and summing each response to repeated



**Figure 1-1.** Dawson's photographic summation to extract EP. Superimposing a number of responses, though each response was variably contaminated by ongoing noise, brought out the response time locked to the stimulus. (From Dawson GD. Cerebral responses to electrical stimulation of peripheral nerve in man. *J Neurol Neurosurg Psychiatr* 1947;10:134–140, with permission.)



**Figure 1-2.** Dawson's electronic summation-averaging technique. Cerebral responses from scalp electrodes after repetitive ulnar nerve stimulation at one per second. By summing and then averaging the responses, the "noise" unrelated to the stimulus can be decreased and the responses can be extracted. (i) is from multiple original tracings and (ii) is obtained after summation—averaging. A is from contralateral and B is from ipsilateral scalp electrodes to the side of stimulation. C is calibration signal. (From Dawson GD. A summation technique for detecting small signals in a large irregular background. *J Physiol* 1951;115:2, with permission.)

sensory stimuli, and dividing the sum by the number of responses. The improvement of signal-to-noise ratio is proportional to the square root of the number of stimuli ( $S/N = k \times \sqrt{N}$  where  $k$  is the  $S/N$  ratio of a single sweep and  $N =$  the number of responses and  $n =$  the number of stimuli). This indicates that a low amplitude response (signal) or high noise level requires a greater number of averages to improve the signal-to-noise ratio (Fig. 1-4). If, for example, you have averaged 100 electrical stimulations and the response is not clear, you will have to go to 400 trials to improve the signal by a factor of 2 and 1,600 trials if you wish to double the improvement again. You may want to consider other methods of improving the  $S/N$  ratio, such as relaxing the patient, filtering, and adjusting the gain. The exception to the square formula is a brief artifact, such as a QRS pulse. In these instances, the noise decreases linearly with the number of trials.

## DIGITAL PROCESS

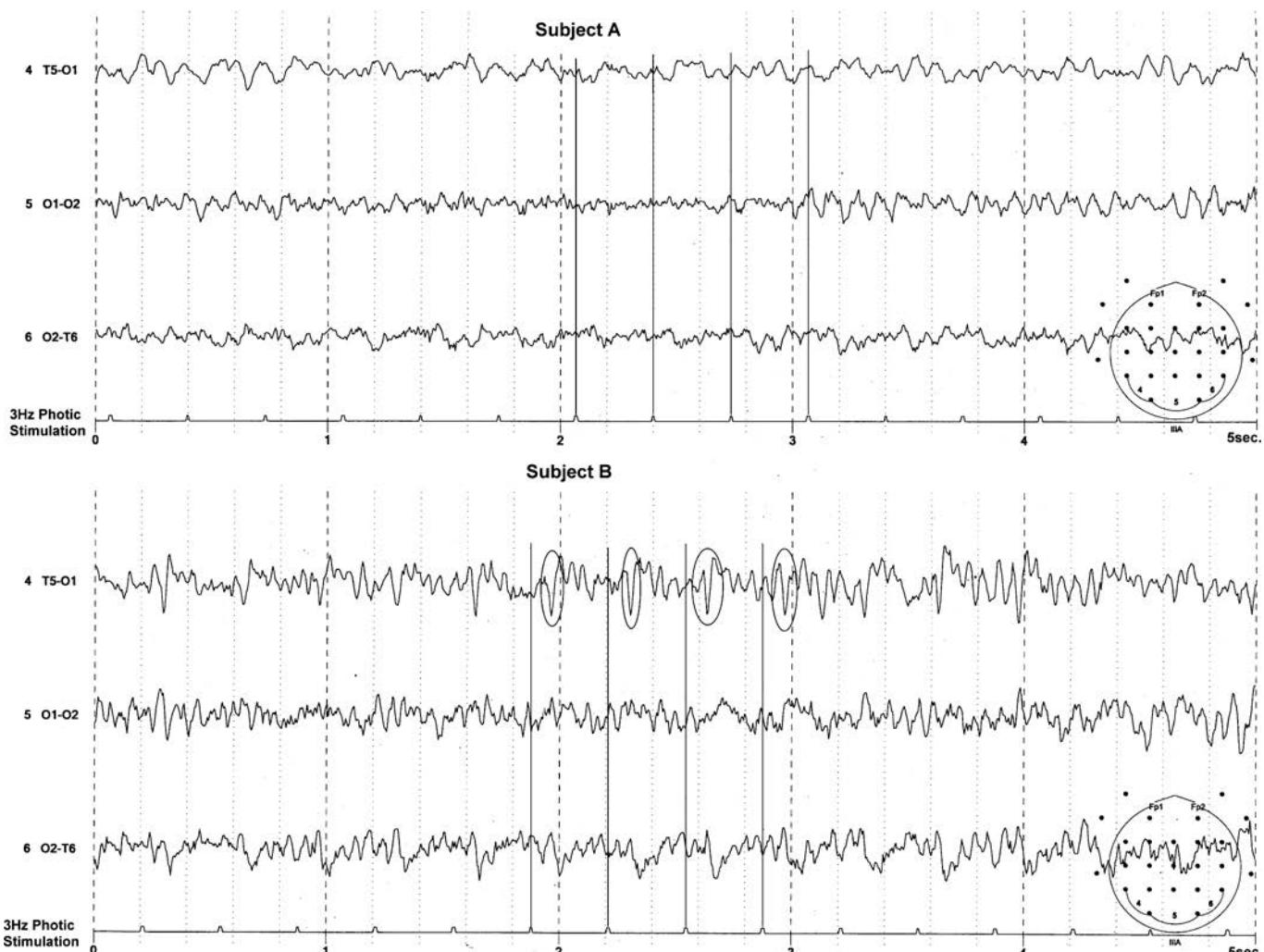
Each analog wave form must be digitized in order to store data points in the computer for signal averaging (Fig. 1-5). This involves vertical (voltage) and horizontal (time) digitization. The vertical resolution depends on the gain factor of the amplifier and "bit" (binary digit) capacity of the analog-to-digital (A/D) converter. The horizontal resolution is expressed by the intersample interval, dwell time, or frequency.

### VERTICAL (VOLTAGE) RESOLUTION AND RANGE

The A/D converter has two parameters that affect amplitude. The Range of an A/D converter is the largest signal that the converter can convert. The Resolution is related to how small a

change the A/D converter will detect. A commercial A/D converter usually has voltage limits (Range) of  $\pm 1$  to  $\pm 10$  V. For example, an A/D converter may have a range of  $\pm 5.12$  V (10.24 V total). The precision of the amplifier depends on how finely the range is divided. To find out how much resolution is required, consider measuring the distance. Do you need to have the measurement precision high enough to measure to the nearest meter? centimeter? millimeter? The same question arises in electrical measurements. The number of bits used to represent the measurement determines the precision (Fig. 1-6A,B). 8-Bit converters were common when people first attempted digital EEG. Using 8 bits, the range is divided into  $2^8$  or 256 levels;  $10.24\text{ V} \div 256 = 0.04\text{ V}$  will be the steps in the conversion. This implies that you would be able to detect changes as small as  $0.04\text{ V}$ . However, this is  $40,000\text{ }\mu\text{V}$ . The EEG would never be large enough to exceed one step; it would convert as a flat line. To overcome this, an amplifier is added to the input of the A/D. What minimum voltage would you like to detect? Since some EPs may be less than  $1\text{ }\mu\text{V}$ , we would like to be able to see changes as low as  $\frac{1}{4}\text{ }\mu\text{V}$  (see Fig. 1-6A). How much gain is required to boost the  $\frac{1}{4}\text{ }\mu\text{V}$  signal to the  $40,000\text{ }\mu\text{V}$  required for one step of the A/D?  $40,000 \div \frac{1}{4}$  is a gain of 160,000. This gives you the resolution to view very small amplitude changes. However, the addition of this amplification also changes the Range! The steps are now  $\frac{1}{4}\text{ }\mu\text{V}$  and there are 256 of them. The range is now  $\frac{1}{4} \times 256 = 64\text{ }\frac{1}{4}\text{ }\mu\text{V}$  totally or  $\pm 32\frac{1}{8}\text{ }\mu\text{V}$ . This will limit the maximum input to  $32\text{ }\mu\text{V}$ ; activity greater than  $32\text{ }\mu\text{V}$  cannot be resolved with an 8-bit A/D converter.

Instead of increasing the gain factor of the amplifier, another solution is to increase the number of bits. Now the range is divided into  $2^{16}$  or 65,536 levels (see Fig. 1-6B). Dividing the range of 10.24 V by 65,536 results in each step being  $0.00015625\text{ V}$  or  $156.25\text{ }\mu\text{V}$ . How much gain would it take to boost the  $\frac{1}{4}\text{ }\mu\text{V}$



**Figure 1-3.** EEG responses to repetitive photic stimulation in two normal subjects. In subject A, there was no visible response to each photic flash but in subject B, discernible response to each flash, mixed with ongoing EEG activity, could be recognized.

signal to 156.25? The gain would need to be 625. Again, the gain affects the range. This time, there are 65,536 steps of  $\frac{1}{4} \mu\text{V} = 16,384 \mu\text{V}$  ( $\pm 8,192 \mu\text{V}$ ). The 16-bit A/D converter with gain of 625 will digitize the signal to the closest  $\frac{1}{4} \mu\text{V}$  and can handle an amplitude up to  $8,192 \mu\text{V}$ !

The amplitude is more faithfully reproduced when a greater number of bits are available (Fig. 1-7).

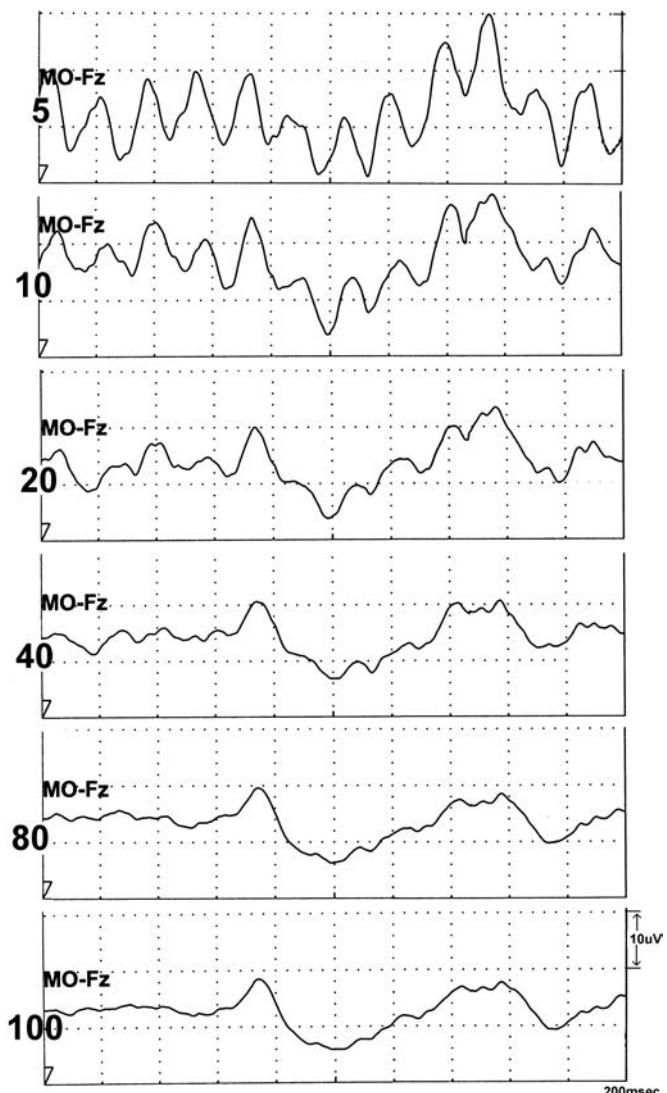
#### HORIZONTAL (TIME) RESOLUTION

Horizontal resolution depends on the number of addresses available per channel and the time for analysis (sweep time). The computer stores the voltage value at each address or digitized time interval, which is called the *intersample interval* or *dwell time*. The faster the sampling rate or the greater the number of addresses available per channel, the shorter the intersample interval, thereby gaining higher resolution (Fig. 1-8). Generally,  $2^9$  (512) to  $2^{12}$  (4,096) addresses should be available for each channel. The American Clinical Neurophysiology Society (ACNS)<sup>3</sup> guidelines recommend at least 500 addresses of memory per channel. The dwell time or the intersample interval is

calculated by the following formula: Dwell time = Sweep time/number of intervals. For example, a sweep time of 240 ms with available addresses of 13 digitized points (12 intervals) is equal to a 20-ms sampling rate (240 ms/12 intervals = 20 ms).

Horizontal resolution may also be expressed as frequency (Hz), as shown by the following formula: Frequency = 1,000 ms/dwell time (Fig. 1-9). For example, the intersample interval or the dwell time of 20 ms corresponds to 50-Hz resolution (1,000 ms/20 ms = 50 Hz).

The time resolution required to preserve the frequency content of a waveform is based on the *Nyquist theorem*. Half the sampling rate (in Hz) of the digitized points is called *Nyquist frequency*. For example, if the sampling rate (dwell time) is 20 ms (equivalent to 50-Hz resolution), frequency components up to 25 Hz can be reproduced without aliasing. In order to resolve 50-Hz activity, a minimum of 100-Hz resolution is required (Fig. 1-10). In other words, the minimum sampling rate should be at least twice the frequency of the original wave form. If the sampling rate is less than the Nyquist frequency, the result will be a slower-than-original wave (*aliasing*) (Fig. 1-11). In general, a sampling rate of three times the frequency of the original wave form is recommended



**Figure 1-4.** An example of response averaging for VEP. With an increasing number of stimuli, the “noise” progressively decreases and the response becomes clearer (from the top to bottom tracings). The “noise” in this case is 60-Hz artifact that is clearly visible in the top 3 tracings (12 waves/200 ms). The number of summations is indicated on the left side of each response.

by ACNS<sup>3</sup> (see more details in *Practical Guide: EEG*, Chapter 2, pp. 10–11, and Chapter 4).

## AMPLIFIER

The A/D converter should cover a full range of voltages from 5 to 50  $\mu$ V. The common mode rejection should be at least 10,000:1 (80 dB)<sup>3</sup> (see also *Practical Guide: EEG*, Chapter 4). The noise level of the amplifier should not exceed 2  $\mu$ V and the available range of band pass should be from 0.1 to 5,000 Hz.<sup>3</sup>

## FILTER SETTING OF AMPLIFIER

An appropriate use of analog filtering is important to optimize the EP recording of interest by effectively reducing artifacts and unnecessary signals, and improving the signal-to-noise ratio.

Setting the low filter (high-pass filter) at a high level minimizes the artifacts from eye movements, T wave of the EKG complex, sweat gland potential (sweat artifacts), and various movements. Because activity slower than 100 Hz is not a concern for brain-stem auditory evoked potential (BAEP) (which has a frequency range of 500–1,000 Hz), the low filter for BAEP can be as high as 100 Hz, while the high filter should be greater than 1,000 Hz, usually 3,000 Hz (3 kHz). In contrast, visual evoked potential (VEP) (which has a frequency range of 5–10 Hz) requires a low filter of 1 Hz and the high filter may be as low as 100 Hz.

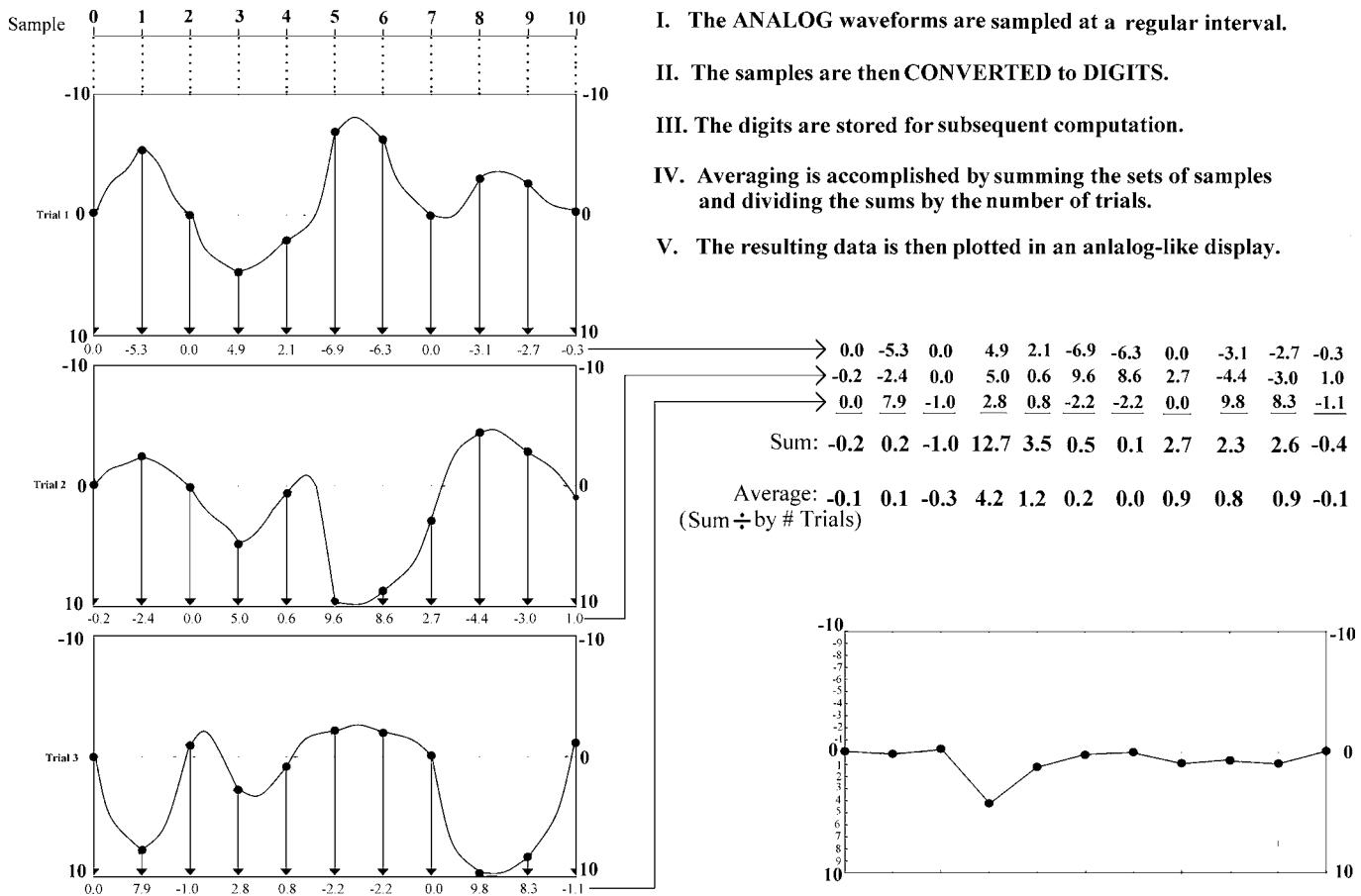
Although the higher low filter and the lower high filter (narrow band filter setting) minimize the artifact contamination allowing faster accumulation of samples by reduced rejection (see auto-rejection-mode), it may cause a loss of the activity of interest (Fig. 1-12). It is also important to realize that changing the analog filter setting alters the peak latency. The peak latency becomes longer with the lower number of high filter setting (Fig. 1-13A–C). Conversely, increasing the number of low filter setting shortens the peak latency (Fig. 1-13B,D). Filter settings, therefore, should not be changed indiscriminately and should be the same as was used when collecting normative data for each modality of EP. In general, the ratio of high-to-low-frequency filter setting should be at least 100:1 to minimize the phase shift.<sup>3</sup>

Use of the 60-Hz notch filter is not recommended although it effectively eliminates 60-Hz artifact. Using the 60-Hz filter may cause “60-Hz ringing” artifact associated with stimulus artifacts or any other large amplitude transient. It consists of rhythmic sine waves with progressively smaller amplitudes following the stimulus artifact, and this may mimic a true response or obscure the short latency component (Fig. 1-14). Since stimulus artifact triggers “60-Hz ringing” and is time locked to the stimulus, it will not average out but rather remain stable as the non-synchronous noise averages out as the number of averages increases. This is problematic for BAEP or somatosensory evoked potential (SSEP), but the 60-Hz notch filter can be used for VEP if 60-Hz artifact cannot be eliminated after technical modification (some cathode ray video screens may generate 60-Hz artifacts when the subject sits close to the screen). The 60-Hz ringing does not occur with VEP because there is no stimulus artifact associated with VEP.

Instead of using the 60-Hz filter, the 60-Hz artifact can be effectively reduced by using a stimulation rate that is not a harmonic number of 60; for example, a stimulus rate of 2.1 or 3.3 instead of the integer value of 2.0 or 3.0 Hz. In fact, some EP instruments automatically adjust to the nonharmonic stimulus rates even if the stimulus rate is set at 2 or 3 Hz. Good electrode application technique as well as low and balanced electrode impedance will also help to minimize 60-Hz artifact.

## AUTOMATIC ARTIFACT REJECTION

Artifact rejection is essential for signal averaging. Without it, artifacts are introduced into the averaged signal. The rejection level is determined by a voltage value; any sample exceeding a predetermined threshold (usually the activity that exceeds the limit of A/D conversion or some adjustable percentage) is assumed to be an artifact and rejected from the average. This is accomplished by examining an overload for each response brought to a buffer. If not overloaded, the response is added to



**Figure 1-5.** The schematic model of analog-to-digital conversion and summation-averaging technique. Each response contaminated by a spontaneous or an ongoing “noise” is digitized and digitized points are stored in the computer. Each digitized point is summed and divided by the sum of number of trials. With this technique, the “noise” unrelated to the stimulus decreases and the “signal” (response) that is time locked to the stimulus remains constant as the number of summations’ averaging increases.

the previously accumulated response and the trial number is incremented by 1. If the buffer contents exceed the threshold, the response is discarded and the rejection number is incremented by 1. This can be switched on or off and the threshold level can be changed in most signal processors. The amount of rejection can also be controlled by changing the gain factor of the amplifier. When uncontrollable artifact causes excessive sample rejection, lowering the gain reduces the number of rejections. When the gain is reduced too low, however, the samples contaminated by artifacts are accepted into the average, which will result in a noisy response. It is important to use a gain setting that will allow the utilization of the full range of voltages in the A/D converter. Therefore, the gain should not be reduced indiscriminately. Generally, the amplifier gain is optimally increased to the state in which approximately 10% to 20% of the total samples are rejected. If the response appears to be “noisy” because of artifact contamination, do not hesitate to increase the number of averaging samples.

## DATA MEASUREMENT AND OFFLINE ANALYSES

The amplitude and latency values are automatically displayed by moving a cursor to the points of interest over the waveforms

that are displayed on the video monitor screen. Using two cursors, the peak-to-peak amplitude or the interpeak latency can be displayed. It should be possible to display waveforms recorded by separate trials in separate memory blocks and superimpose them to assess the intertrial variability or the repeatability of the response. They may be averaged together, added, or subtracted from one another as an offline procedure. Using subtraction, it is possible to generate a new derivation if two different channels have a common electrode. For example, subtraction of F3-A1 in one channel from C3-A1 in another channel can create C3-F3 [(C3-A1) - (F3-A1) = C3-F3]. Some averagers offer a “zoom” capability that allows a restricted section of a sweep to be expanded for detailed examination and measurement. If the system has two digitizers, two different sweep times in separate memory blocks can be recorded simultaneously.

Unlike analog filtering that may alter the peak latencies when changing the filter setting, digital filters can be designed so that they do not produce phase/latency shift (Fig. 1-15). (It should be noted that the digital filter can also be designed to mimic an analog filter. See *Practical Guide: EEG*, Fig. 2-17.) It can be a convenient technique in identifying and emphasizing the small fast frequency peaks riding over the slow potential by raising the low-frequency filter setting beyond what was originally used (Fig. 1-16). Conversely, a response contaminated by

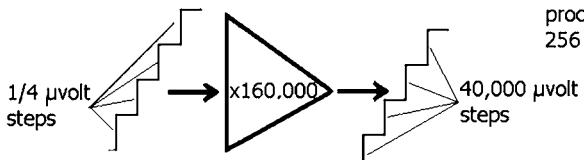
## 8-Bit A/D Converter

### Converter Characteristics

Range:  $\pm 5.12$  volts = 10.24 volts (peak-peak)  
 Resolution: 8-Bit  $> 2^8$  levels = 256 Steps  
 Voltage Resolution:  $10.24$  volts  $\div 256$  =  
0.04 volts or 40,000 μvolt steps.

Since evoked potentials may be less than 5  $\mu$ volt, being able to detect a  $1/4$   $\mu$ volt change would be desirable. To increase the resolution to  $1/4$   $\mu$ volt steps, an amplifier is added to boost the  $1/4$   $\mu$ volt step to 40,000  $\mu$ volt.

Dividing the output by the input ( $40,000$  by  $1/4$ ), the amplification would have to be 160,000. This shifts the resolution to  $1/4$   $\mu$ volt; a  $1/4$   $\mu$ volt change becomes a 40,000  $\mu$ volt change and the A/D changes its output by one step.

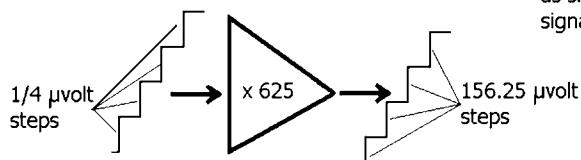
**A**

## 16-Bit A/D Converter

### Converter Characteristics

Range =  $\pm 5.12$  volts = 10.24 volts (peak-peak)  
 Resolution: 16 bit  $> 2^{16}$  levels = 65,536 steps  
 Voltage Resolution:  $10.24$  volts/ $65,536$  steps  
 $= 0.000015625$  volts =  $156.125 \mu$ volt.

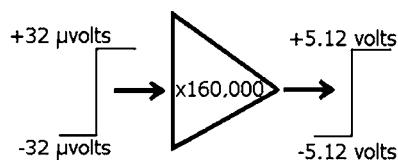
The goal of recording with the ability to detect  $1/4$   $\mu$ volt changes in the input signal remains the same. Again an amplifier is added. However this time the 10.24 volt range is divided by 65,536 steps of  $156.125 \mu$ volt each. The amplification required to boost  $1/4$   $\mu$ volt to  $156.125 \mu$ volt is much less:  
 $156.25 \div 1/4 = 625$ .

**B**

The addition of an amplifier changed the resolution to  $1/4$   $\mu$ volt. The amplifier also changed the range.

The range of the A/D by itself is  $\pm 5.12$  volts: A  $+5.12$  volt input signal will drive the A/D to its upper limit (i.e. 11111111) while a  $-5.12$  volts will drive it to its lower limit (00000000). With the gain of 160,000, applying  $1/160,000$  of  $+5.12$  volts to the amplifier input will result in  $+5.12$  volts at the A/D.  $5.12 \div 160,000 = 0.000032$  volts or  $32 \mu$ volt. The range now is  $\pm 32 \mu$ volt. The input signals will be accurately converted if they are between  $-32$  and  $+32 \mu$ volt (64  $\mu$ volt peak-peak)

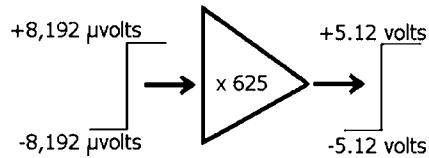
Another way to determine the range: We know that  $1/4$   $\mu$ volt change at the input produces a step change. There are 256 steps.  $256$  steps  $\times 1/4$   $\mu$ volt/step =  $64 \mu$ volt range.



Again the addition of an amplifier changes the range as well as the resolution.

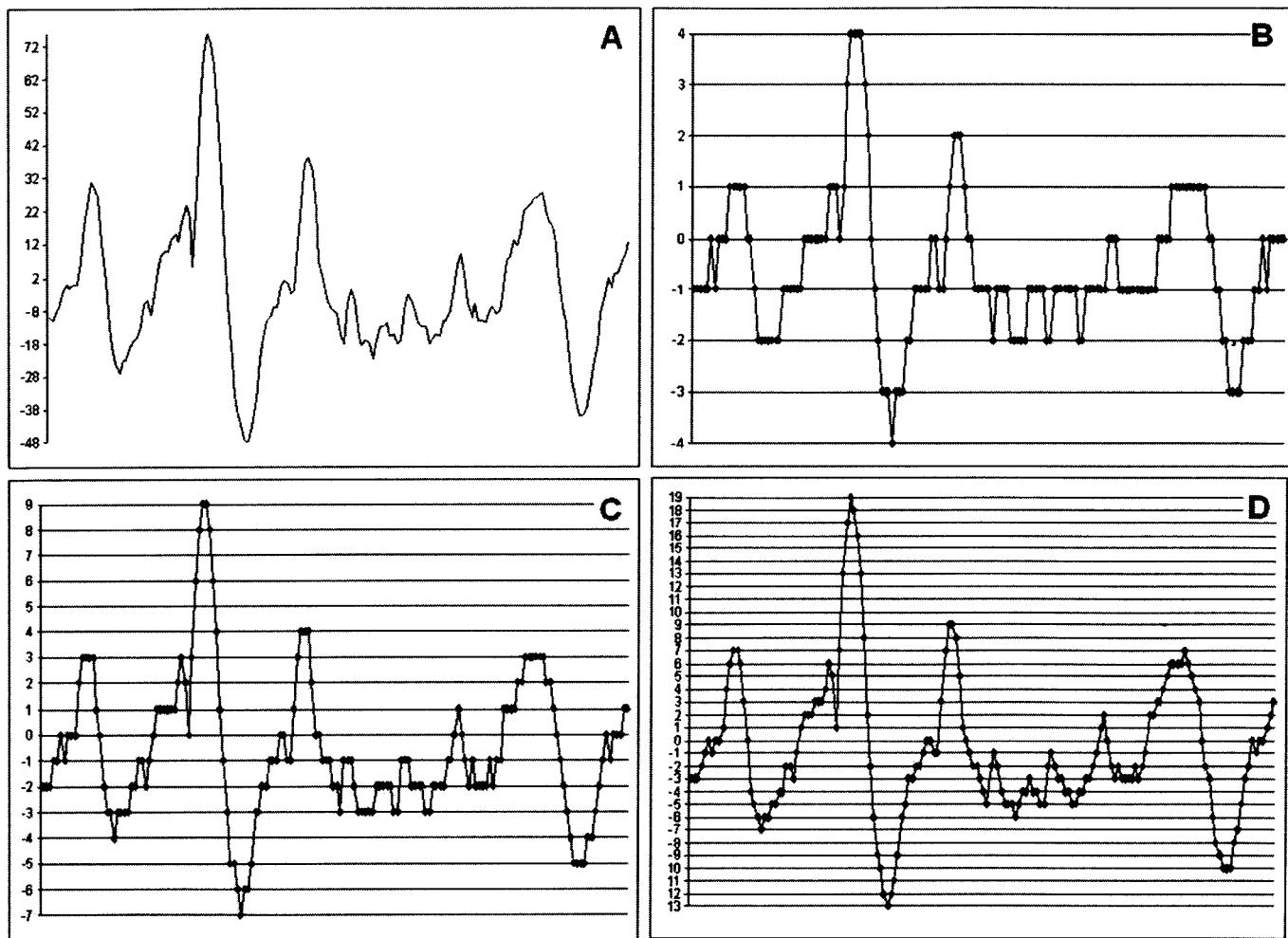
The range of the A/D by itself is still  $\pm 5.12$  volts. The gain of 625 means that it will take only  $1/625$  of 5.12 volts to drive the A/D output to its upper limit (1111111111111111). And  $1/625$  of  $-5.12$  volts to drive it to its lower limit (0000000000000000). The range is now  $1/625 \times \pm 5.12$  volts =  $\pm 0.008192$  volts or  $\pm 8,192 \mu$ volt.

The combination of an amplifier and a 16-bit A/D converter allows the detection of changes as small as  $1/4$   $\mu$ volt while tolerating input signals from  $-8,192$  to  $+8,192 \mu$ volt.

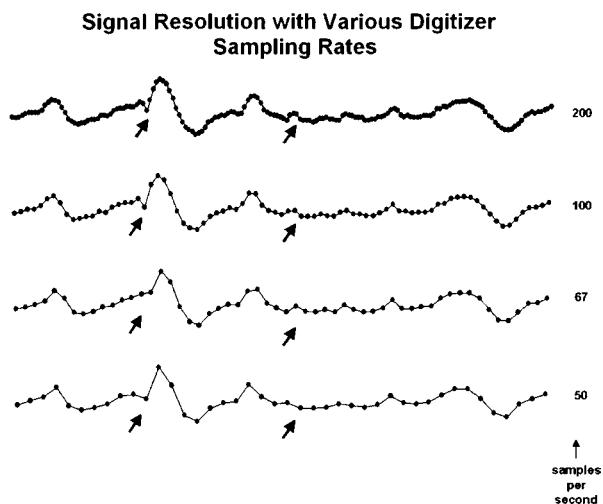


**Figure 1-6.** Examples of A/D converter limitation. Assuming that A/D converter has 8 bits with  $\pm 5.12$  V range (10.24 V for full range), this allows 40,000  $\mu$ V for one-step resolution (A). In order to register one step for  $0.25(1/4)\text{-}\mu$ V signal, this signal must be amplified 160,000 times. With this amplification, the maximum amplitude of signal that can be registered is 64  $\mu$ V or  $\pm 32 \mu$ V. If A/D converter has 16 bits with  $\pm 5.12$  V range (10.24 V for full range), only 625 times amplification allows to register 0.25  $\mu$ V signal and also maximum amplitude of signal can be increased to 16,384  $\mu$ V or  $\pm 8192 \mu$ V (B).

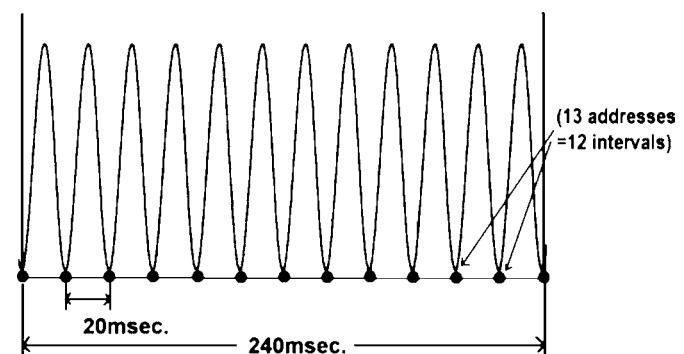
## Amplitude Resolution with Different Amplitude Ranges



**Figure 1-7.** Wave form alteration depending on the amplitude resolution. **A** is the original signal. The greater the number of steps (bit number), the more detailed the response created (**B** to **D**).



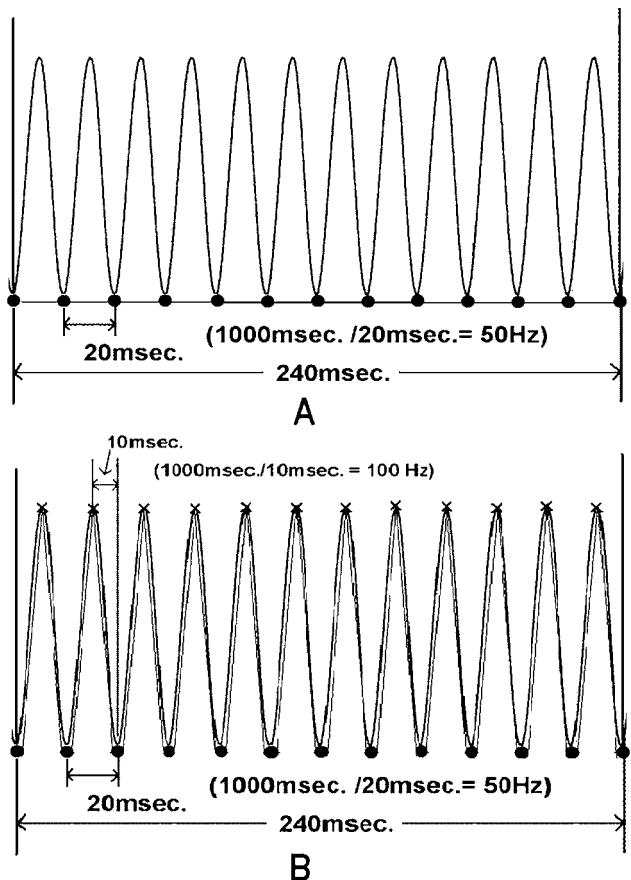
**Figure 1-8.** Signal resolution with various sampling rates. The greater the number of samples available, the greater the resolution. Note small notched waves visible with 200 samples (shown by arrows) per second are lost with 50 samples per second.



$$\text{Dwell time} = \text{sweep time} / \# \text{intervals} = 240/12 = 20 \text{ msec.}$$

$$\text{Frequency} = 1000 \text{ msec.} / \text{dwell time} = 1000 \text{ msec.} / 20 \text{ msec.} = 50 \text{ Hz}$$

**Figure 1-9.** Example of sampling rate or dwell time in relationship with analysis time. With 240-ms analysis time, 50-Hz sampling rate is equivalent to 20 ms dwell time.



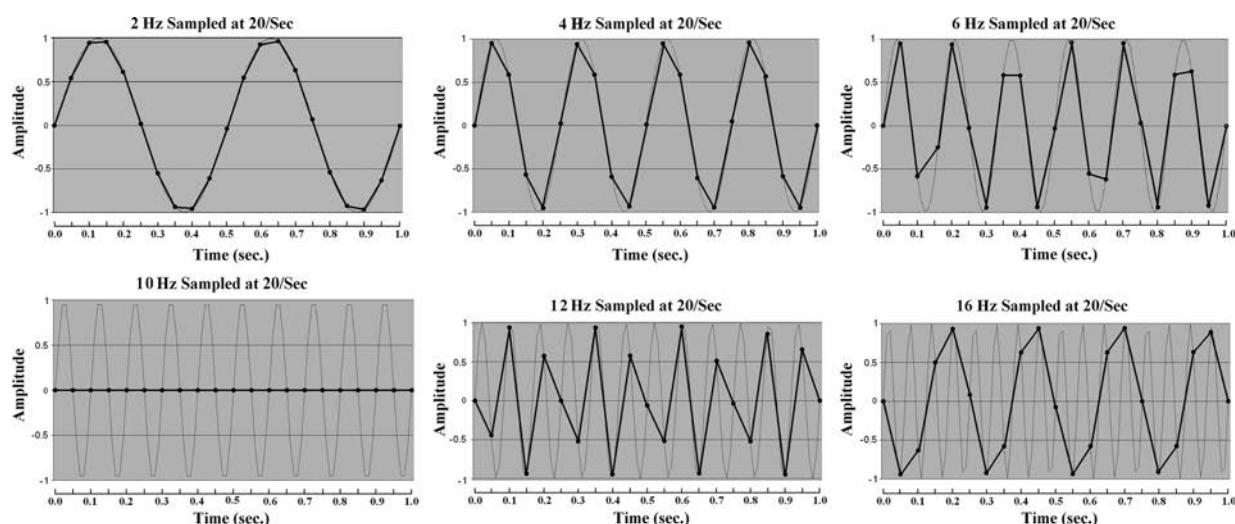
**Figure 1-10.** Example of minimal sampling rate to resolve 50-Hz activity. If the available sampling rate is 20 ms (shown by closed circle), this would result in “flat” tracing by connecting the available dots (A). In order to reproduce 50-Hz activity, shortening the sampling rate (dwell time) is necessary by adding more points (shown by X mark) with 10-ms intervals (B). This is equivalent of 100-Hz resolution, that is, the resolution of at least twice the frequency of the original wave form is required.

high-frequency “noise” can be better visualized with the use of the high-frequency filter or using a “smoothing” algorithm (Fig. 1-17). Smoothing is accomplished by averaging the neighboring data points, thereby creating a new data point at each digitized point. However, it should be noted that excessive smoothing may eliminate fast components of interest or lose the detail of the wave form.

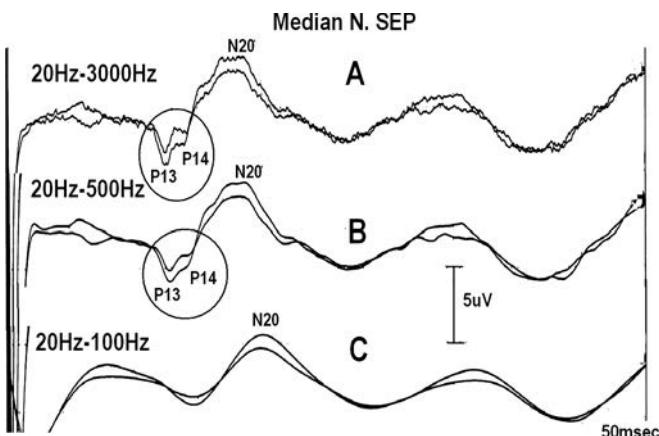
The stored wave form data can be quantified by the use of computer programs such as amplitude or power spectrum topographic mapping, auto- and cross-correlation or covariance.

## POLARITY CONVENTION

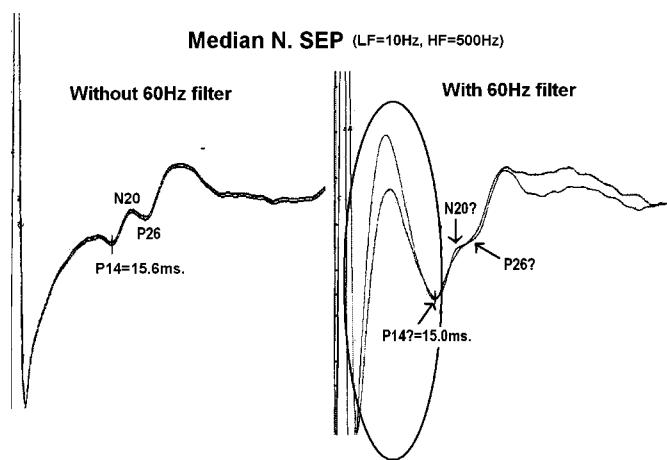
Similar to the EEG instrument, signal averagers use differential amplifiers. However, the polarity convention of some commercially available signal averagers may be opposite to that of EEG such that if input 1 is relatively more positive as compared to input 2, it results in an upward deflection. In this setting, to express upward deflection as positive polarity (as commonly used for waves I through V of BAEP), the active electrode (Cz) is connected to input 1 and the reference electrode (A1 or A2) is connected to input 2. On the contrary, since P100 of VEP is usually expressed as a downward deflection, the reference electrode (A1 or Fz) must be plugged into input 1 and the active electrodes (occipital electrodes) are in input 2. Technologists must be cautious in preparing this confusing input convention for the EP recording. If there is a mistake (i.e., the wave form turns upside down), a normal response can be easily misinterpreted as abnormal or vice versa. Although most laboratories use upward deflection as a positive polarity for BAEP and as a negative polarity for VEP and SSEP, there is no universal standard. It is, therefore, important to indicate polarity on the figures by labeling them “+” or “-,” or stating “positive up” or “negative up” in the legend.



**Figure 1-11.** Examples of “aliasing” due to insufficient sampling rates. Using available digitized sampling points of 20 per second (20-Hz sampling rate) or 50 ms dwell time, 2, 4, 6, 10, 12, and 16 Hz sine waves are reproduced. The activity less than 10 Hz (half of the sampling rate) can be faithfully reproduced though the wave forms are more distorted with the higher frequency activity. The 10-Hz activity become “flat” and the activity faster than 10 Hz can no longer be reproduced, becoming a slower frequency than the original signal.



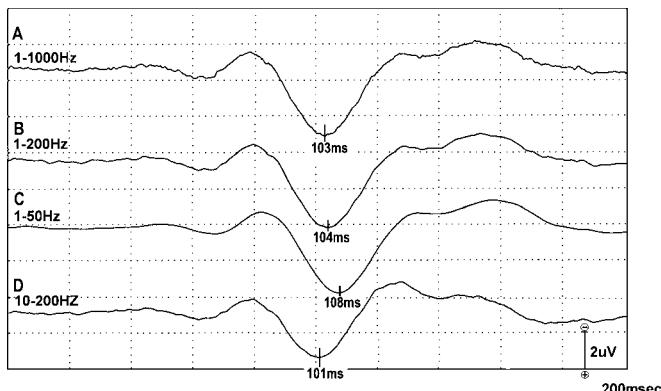
**Figure 1-12.** An example of lowering high-frequency filter setting causing loss of details of fast frequency activity, although the response appears “cleaner.” In this case, P13 and P14 far-field potentials of SSEP (shown by circles in A and B) registered with high filter setting of 3,000 or 500 Hz are lost by reducing high filter setting to 100 Hz (C).



**Figure 1-14.** An example of 60-Hz “ringing” showing large sinusoidal artifact after the stimulus (shown by oval circle). This often causes rhythmic sinusoidal waves with progressively decreasing amplitude after the stimulus artifact. Because this is time locked to the stimulus, it may be mistakenly interpreted as a true response or it may obscure the short latency components occurring shortly after the stimulus. Because of contamination of large 60-Hz “ringing” artifact, it is not certain if the initial positive deflection represents P14. Also, N20 and P26 peaks are obscured.

## WAVE FORM NOMENCLATURE

Wave form nomenclature is another confusing matter in dealing with EP studies. There are essentially two methods: (i) numbers in sequence preceded by polarity, for example, N1, P1, N2, P2, etc., or (ii) polarity and mean latency from normal subjects, for example, P14, N20, P100, etc. BAEP is often expressed in sequential Roman numerals, waves I through V. VEP is expressed as N1, P1, N2 or more commonly as N75, P100, N145. SSEP is usually expressed by polarity and mean latency of normal population. Since SSEP latency values linearly change along with the arm length or height, N18, for example, cited in Japanese literature may be equivalent to N20 used in American or European literature.



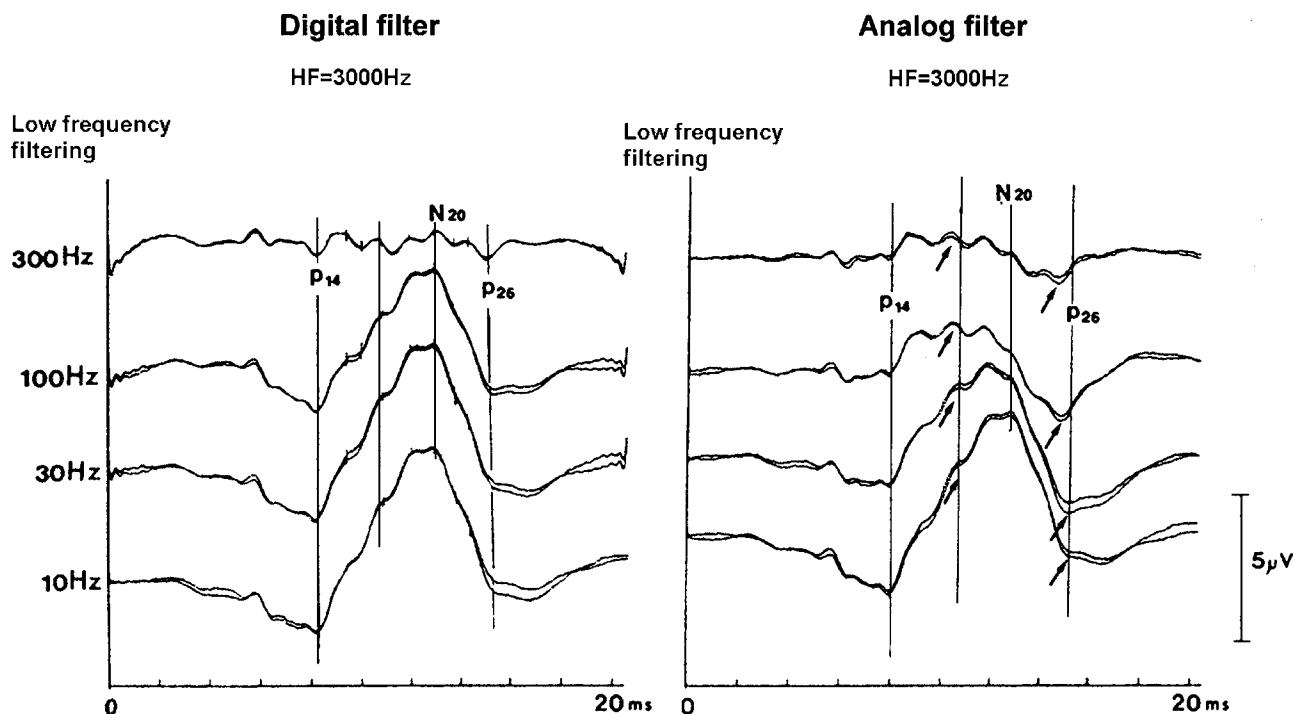
**Figure 1-13.** Examples of latency alteration by changing filter setting. The P100 latency of VEP recorded with low filter (LF) setting of 1 Hz and high filter (HF) setting of 1,000 Hz (control) (A) becomes longer with the decreasing high filter setting (B and C). Conversely, P100 latency becomes shorter by increasing the low filter setting (compare B and D).

## DETERMINATION OF NORMALITY AND ABNORMALITY

The abnormalities in EPs are primarily determined by amplitudes and latencies. These are assessed by their absolute and relative values, and their deviations from normal data are considered to be abnormal. The normative data are determined by mean and standard deviation (SD) values from a group of normal individuals. If the values have a normal distribution, that is, a Gaussian distribution, abnormality can be determined if the value is greater than 3 or 2.5 SD beyond the mean (Fig. 1-18). The confidence level is 99.7% for 3 SD and 98.8% for 2.5 SD. For example, if the mean latency and its SD are 10.5 ms and 1.2 ms, respectively, a value greater than 14.1 ms [ $10.5 + (3 \times 1.2)$ ] or less than 6.9 ms [ $10.5 - (3 \times 1.2)$ ] is considered to be abnormal. In physiological measure, an abnormality is determined by the longer but not by the shorter latency in most of the conditions.

The latency value of EPs has a Gaussian distribution; therefore, a deviation greater than 2.5 or 3 SD from the mean can be used in determining latency abnormalities. However, most amplitude values have a non-Gaussian distribution (with a steeper curve on the low-amplitude side than on the high-amplitude side) with large SD values. For example, if the mean and the SD values are 10  $\mu$ V and 4  $\mu$ V, respectively, even the negative value [ $10 - (4 \times 3) = -2 \mu$ V] falls within the normal limit value. Therefore, an amplitude abnormality value is roughly determined based on experience and an arbitrary estimate, for example, a difference greater than 50% between the left and right sides within the same individual may be considered abnormal.

Amplitude is often measured from peak to peak (negative peak from preceding positive peak or vice versa). The amplitude value (expressed as “+” or “-”) may also be measured from the baseline (or “0” potential line). The mean amplitude value

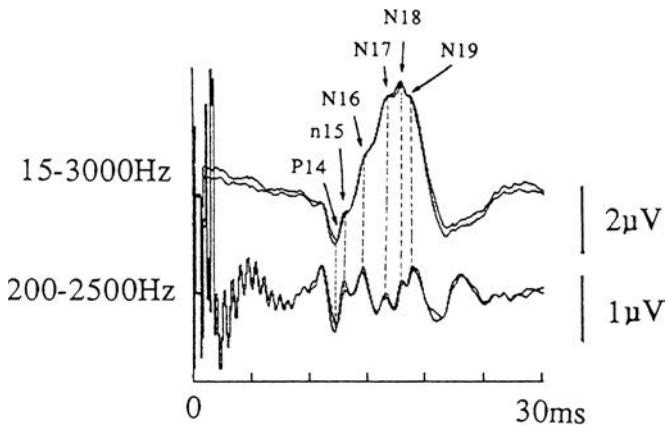


**Figure 1-15.** A comparison between digital and analog filtering. Note the latency of the small notched wavelets (shown by vertical lines) remains the same irrespective of digital low filter settings (10–300 Hz). In analog filtering, however, the latencies of some small wavelets become shorter with the higher low filter setting as shown by arrows, while others (e.g., P14 and N20) remain the same.

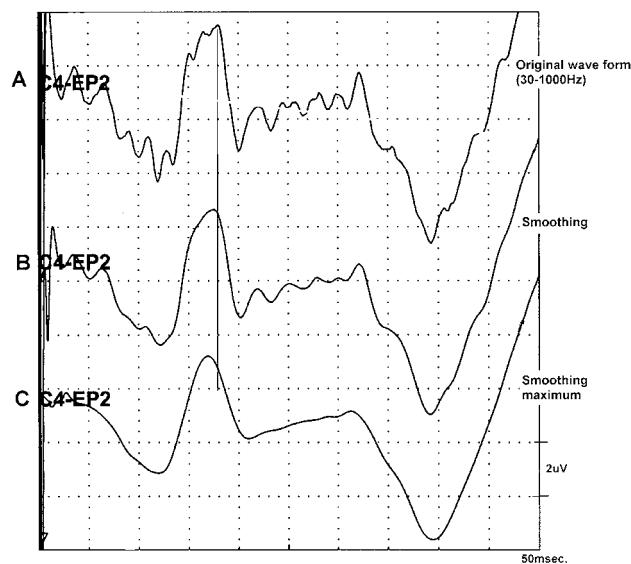
of each digitized point of the entire wave form can be derived from the sweep time. If the EP is recorded including a small fraction of prestimulus time, the mean value of the prestimulus data can be used as a baseline. Even with the use of a prestimulus baseline, expressing the amplitude as a positive or negative

value may be problematic if the tracing has a baseline shift due to a large stimulus artifact.

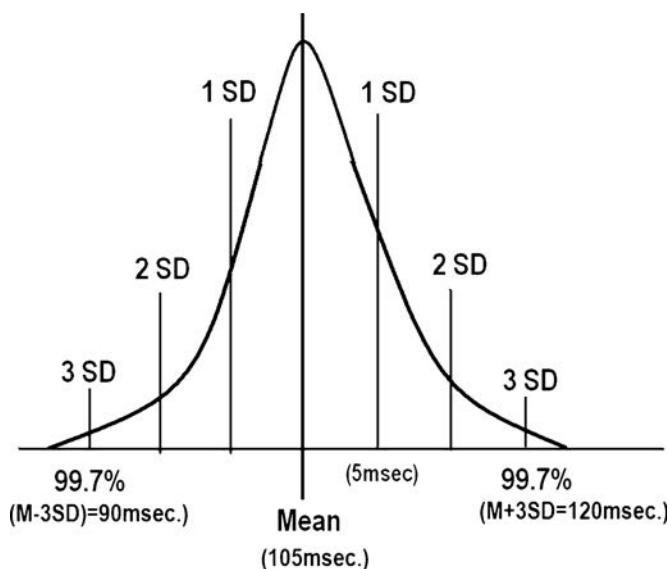
In establishing normal data, age difference must be taken into account. P100 latencies of VEP, for example, tend to increase with advancing age. Therefore, normal data of about ten subjects



**Figure 1-16.** An example of digital filtering to enhance fast activity (frequency close to 1,000 Hz) over-riding slow (about 150 Hz) activity. Changing the low filter setting from 15 to 200 Hz (which will attenuate activity slower than 200 Hz.) and increasing the amplitude scale enable better visualization of ultrafast activity (see Chapter 4, page 57, High Frequency Oscillation (HFO) of SSEP).



**Figure 1-17.** An example of using “smoothing” algorithm for “noisy” SSEP response. Note the decrease of high-frequency noise (likely muscle artifacts) in the original tracing (A) as the “smoothing” is applied (B and C). This effectively eliminated “noise”, changing “noisy” response to “smooth” wave form, while maintaining basic wave form (the latency may vary slightly depending on the “noise” level).



**Figure 1-18.** A Gaussian distribution showing a mean of 105 ms and an SD of 5 ms Abnormality with 99.7% confidence is defined as Mean  $\pm$  3 SD. In this sample, the lower limit of normal is [105 ms  $- (3 \times 5 \text{ ms}) = 90 \text{ ms}$ ] and the upper limit of normal is [105 ms  $+ (3 \times 5 \text{ ms}) = 120 \text{ ms}$ ].

from each decade must be obtained. Except for children less than 2 years old, the age factor can be ignored for BAEP. In the pediatric population, (especially <2 years old), all EPs show considerable maturational differences; therefore, normal data based on conceptional age must be obtained with greater detail in the younger age groups, especially for premature babies. After the age of 2 years, normal data of VEP and BAEP show values close to those of adult values. SSEP latency values after 2 years of age depend on the height and arm length. Therefore, normal data based on height for lower extremity SSEP and arm length for upper extremity SSEP need to be established.

Minor gender differences were found in BAEP and VEP, but the differences are minimal and do not need to be considered for routine clinical EP examination.

Statistically significant abnormalities may be found when two groups of the population are compared, for example, a normal group versus a group of a particular disease, even if the individual values from the disease group are within normal limits.

Because there are differences in instruments, recording parameters, environments, and populations studied among different laboratories, each laboratory needs to establish its own normative data, testing 30 to 50 normal subjects. Greatest interlaboratory differences are found in VEP. This is mainly due to the differences in pattern luminance and constant, ambient room illumination, check size, screen size, etc. Interlaboratory differences appear to be smallest in BAEP, allowing the use of other laboratory's normal data if the recording and stimulus parameters are the same.

## TECHNICAL PROBLEMS IN RECORDING EPs

Technical problems in recording EPs are more common and often difficult to solve than in recording EEG. Technical mistakes or technically suboptimal responses could lead to

serious misinterpretation of the EP results. Following are some commonly encountered problems with some advice for obtaining a solution.

### NO APPRECIABLE RESPONSE

1. Is the stimulus adequately delivered to and perceived by the patient?
2. Check the amplifier gain, filter settings, and integrity of the cable connections.
3. Check the recording parameters (sweep time, electrode derivations, horizontal or vertical scale, amplifier gain, etc.)
4. Is the stimulus appropriately triggering the sweep?

### “NOISY” RESPONSES

1. If muscle or movement artifacts are not adequately controlled due to lack of patient’s cooperation, increase the number of summations. Also increase the number of trials so that three or more responses can be compared and superimposed. A grand average of responses can be obtained by adding all responses offline.
2. Low electrode impedance is important to minimize the contamination of 60 Hz or other nonphysiological interference patterns.
3. Lower the high filter or raise the low filter setting. However, it should be noted that this may alter the peak latency or may attenuate or eliminate the activity of interest.
4. If the source of 60 Hz or other nonphysiological interference pattern cannot be eliminated, try a different stimulus rate so as to avoid a harmonic relationship with the frequency of the interference pattern.

### LARGE STIMULUS ARTIFACTS

1. Check the location of the stimulus cable and the input cable. They should be separated. Keep the recording electrode wires close together.
2. Check the recording electrode impedances. High electrode impedance increases stimulus artifacts.
3. Check the integrity of the ground electrode.
4. Increase the surface area of the ground electrode to decrease its impedance.
5. Lower the stimulus intensity but not to such a degree that the response would be lost.
6. For BAEP, use alternating click polarity (rarefaction and condensation clicks) or add the responses obtained by rarefaction and condensation clicks offline. Be aware that changing click polarity might alter the response, and using alternating polarity may result in a response that is different from either rarefaction or condensation alone.
7. For SSEP, add two responses, each obtained by switching the polarity of the stimulus electrodes. This, too, is not ideal since it may alter the peak latency even if only minimally.

### EXCESSIVE SAMPLE REJECTION (WITH AUTOREJECTION MODE)

1. If the rejection is due to excessive muscle artifact, work on patient relaxation. It may be necessary to sedate the patient. Sedation can be used for BAEP and SSEP testing but not for VEP testing.

2. If stimulus artifact is the source of the rejection, try to reduce it (as described above in “Large Stimulus Artifacts”) or use a few milliseconds of delay time. This delays the start of the averaging process until a few milliseconds after the stimulus; thus, autorejection mode will ignore this amount of time.
3. If the rejection source is a large T wave or EKG complex, raise the low filter (remember this may alter the peak latency).
4. Reduce the sweep (analysis) time if it is unnecessarily long.
5. Adjust the rejection threshold.
6. Reduce the amplifier gain. Excessive reduction of amplifier gain, however, will accept all the samples including

samples contaminated with artifacts, resulting in “noisy” responses.

## REFERENCES

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1. Dawson GD. Cerebral responses to electrical stimulation of peripheral nerve in man. *J Neurol Neurosurg Psychiatr* 1947;10:134–140.
2. Dawson GD. A summation technique for detecting small signals in a large irregular background. *J Physiol* 1951;115:2.
3. American Clinical Neurophysiology Society. Guideline 9A Guideline on Evoked Potentials. *J Clin Neurophysiol* 2006;23(2):125–138.

# Visual Evoked Potentials

## INTRODUCTION

Earlier visual evoked potential (VEP) studies used strobe (flash) light stimulation. This elicits a series of negative-positive deflections consisting of wave I through V within 200 ms after the stimulus (see Fig. 2-14).<sup>1</sup> Although the amplitudes of these waves are robust, inconsistent appearance of individual waves across the subjects makes them difficult to use for clinical diagnostic testing. In contrast, the pattern shift checkerboard stimulation introduced by Halliday et al.<sup>2</sup> elicits consistent responses with relatively simple waveform and minimal inter-individual variability and has been widely popularized for neurophysiologic testing of the visual pathways. Multiple technical factors affect VEP waveforms. It is important for each laboratory to collect its own normal data, using its own stimulator device, recording equipment, and recording parameters.

## ANATOMY OF THE VISUAL SYSTEM

To understand the mechanism and physiology of VEPs, it is important to know the anatomy of the visual pathways (Fig. 2-1). The visual field is divided into temporal and nasal fields, and an input from each field travels through separate pathways. Through the lens, the nasal visual field is projected to the temporal retina and the temporal visual field is projected to the nasal retina. Similarly, the superior and inferior visual fields are inverted. The superior visual field projects to the inferior retina and the inferior visual field projects to the superior retina.

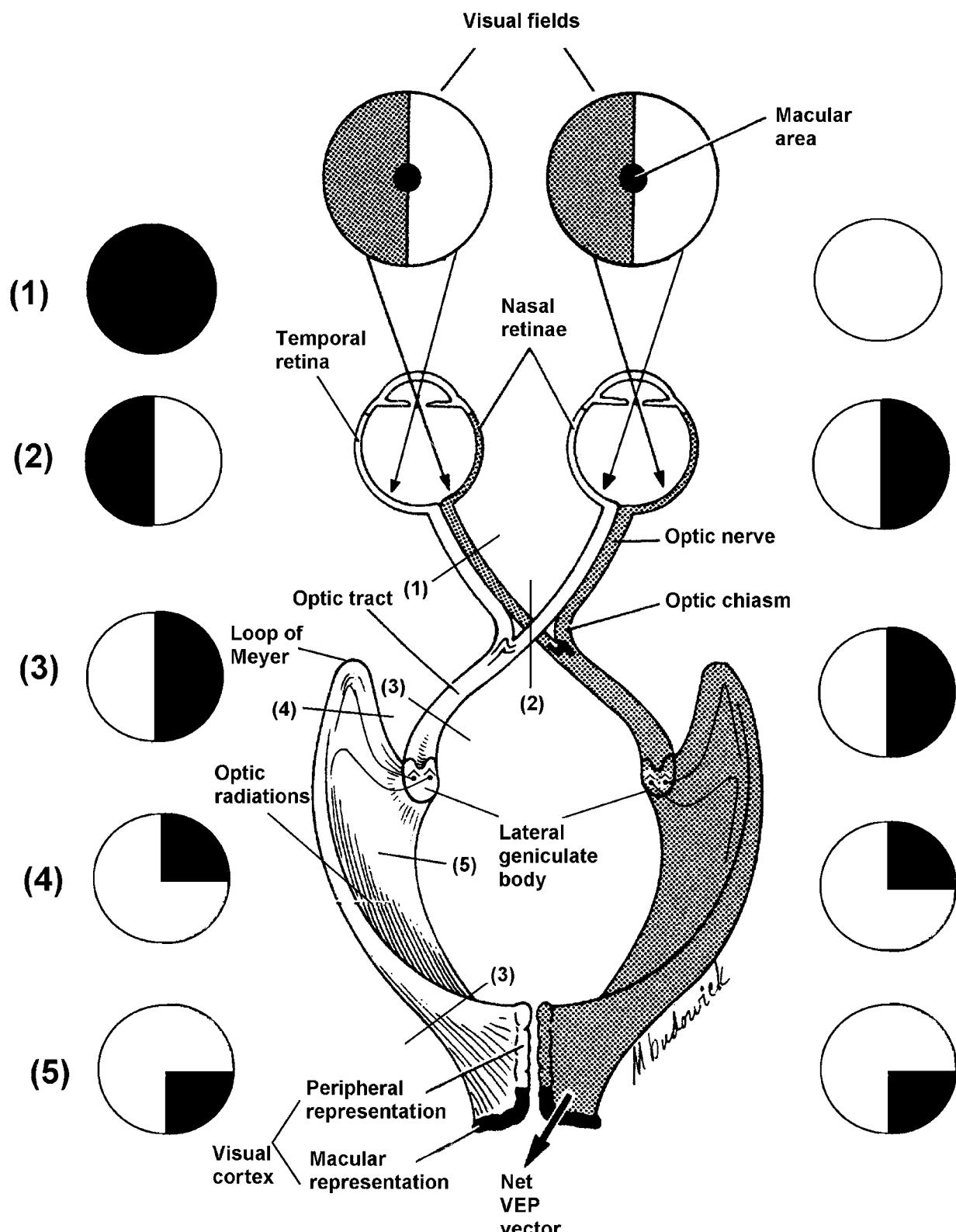
The photo receptor cells in the retina consist of rods and cones. The rods react only to dim light and are found predominantly in the peripheral retina. The cones react to color and are sensitive to bright light. The cones are concentrated in the macular region. The center of the macula, called the foveal pit, is slightly indented and is where the cones are densely packed. This region corresponds to the central 3 degrees of the visual field, providing the highest visual acuity.

The output of the rods and cones projects to the bipolar cells and then to the ganglion cells. The axons of the ganglion cells form the retinal fibers that exit the eyeball as the *optic nerve* (Fig. 2-1). The optic nerves are cranial nerve II and both nerves from the left and right eyes merge at the *optic chiasm*, where the input from the nasal retina (temporal visual field) of each eye crosses to the opposite hemisphere while the input from the

temporal retina (nasal visual field) travels ipsilaterally, forming the *optic tract* after the chiasm. As a consequence, the left optic tract contains fibers from the temporal retina of the left eye and the nasal retina of the right eye (right homonymous visual field), which reflects the right half of the visual field from each eye. Conversely, the right optic tract contains fibers from the temporal retina of the right eye and the nasal retina of the left eye, reflecting the left half of the visual field from each eye (left homonymous visual field). The optic tract enters the *lateral geniculate body* in each hemisphere. After the synaptic connection at the lateral geniculate body, the optic nerve fibers spread widely in the temporal and parietal lobes forming *optic radiations*. The optic radiation from the inferior retina (reflecting the superior visual field) swings toward the tip of the temporal lobe. This is known as the *Loop of Meyers*. The widespread optic radiations converge as they approach the occipital cortex. The primary visual cortex, named *Brodmann area 17*, is situated at the medial occipital cortex and occipital pole, which is also called the *striate cortex*. The central 3 degrees of vision (macular vision) occupy one third of the primary visual cortex, represented at the occipital pole in the posterior portion of the medial occipital cortex. The peripheral visual field is represented in a deeper portion of the medial cortex.

The examination of patterns of the visual field defect allows the localization of a lesion as follows (see Fig. 2-1); lesions are indicated by numbers 1 through 5:

1. An optic nerve lesion causes total blindness of the eye on the affected side.
2. A lesion in the central chiasm (often seen in pituitary tumors) affects optic nerve fibers from the nasal retina of each eye resulting in bitemporal hemianopsia.
3. An optic tract lesion causing complete interruption of the optic tract or optic radiations (postchiasmal lesion) causes a hemifield visual field deficit on the side contralateral to the lesion on each eye, that is, homonymous visual field defect.
4. A lesion partially interrupting the optic radiation in the temporal lobe affecting the Loop of Meyers causes  $\frac{1}{4}$  of a visual field defect in the superior field on the side contralateral to the lesion of each eye, that is, homonymous superior quadrantanopsia.
5. A lesion partially interrupting the optic radiation in the parietal lobe causes  $\frac{1}{4}$  of a visual field defect at the inferior field on the side contralateral to the lesion on each eye, that is, homonymous inferior quadrantanopsia.



**Figure 2-1.** Anatomy of the visual pathway and its relationship to visual fields. Visual input travels from the retina to the optic nerve, optic chiasm, optic tract, lateral geniculate body, and optic radiation and finally reaches the occipital cortex. The left visual field from each eye reaches the right occipital cortex and vice versa. Note that the macular vision, where the highest visual acuity is perceived, is represented in the occipital pole, and the peripheral vision is represented in the more medial surface of the occipital lobe. Injuries to the visual pathway at different locations cause different types of visual field defects. The site of an injury, identified by the number, results in a visual field defect shown with a corresponding number. Conversely, a site of injury can be estimated by examining the visual field defect. (Modified from Snell RS. *Clinical Neurophysiology for Medical Students*, 5th ed. Baltimore, MD: Lippincott Williams & Wilkins, 2001, with permission.)

## TECHNICAL PARAMETERS

### STIMULUS DEVICES

Pattern shift or pattern reversal stimulation is delivered by an electronically controlled video monitor screen or by a mechanical device using a slide projector and a mirror. Although a video monitor takes 20 to 30 ms to fill the screen from top to bottom, there is no significant difference in intersubject variability between projector and video monitor devices.<sup>3</sup> Another stimulus device is light emitting diodes (LEDs).<sup>4,5</sup> Video screens tend to produce longer-latency P100 as compared to LED stimulation. The pattern reversal stimulator typically consists of a black and white checkerboard with sharp contour (Fig. 2-2). Black and white checks reverse at a fixed rate; thus, there is no change in total light luminance. Some laboratories prefer to use a sinusoidal grating contour with gradually changing luminance between light and dark strips.<sup>6,7</sup> Sinusoidal grating stimulus is less affected by refractive errors than checkerboard stimuli. Since black and white checkerboard patterns have been most commonly used in clinical diagnostic testing, this chapter deals only with checkerboard stimulation.

The following stimulus parameters affect P100 amplitude and/or latency: (i) visual angle subtended by the entire screen, (ii) check size, (iii) luminance of the screen, and (iv) contrast. Once these parameters are decided, they should be standardized for all recordings.

### VISUAL ANGLE

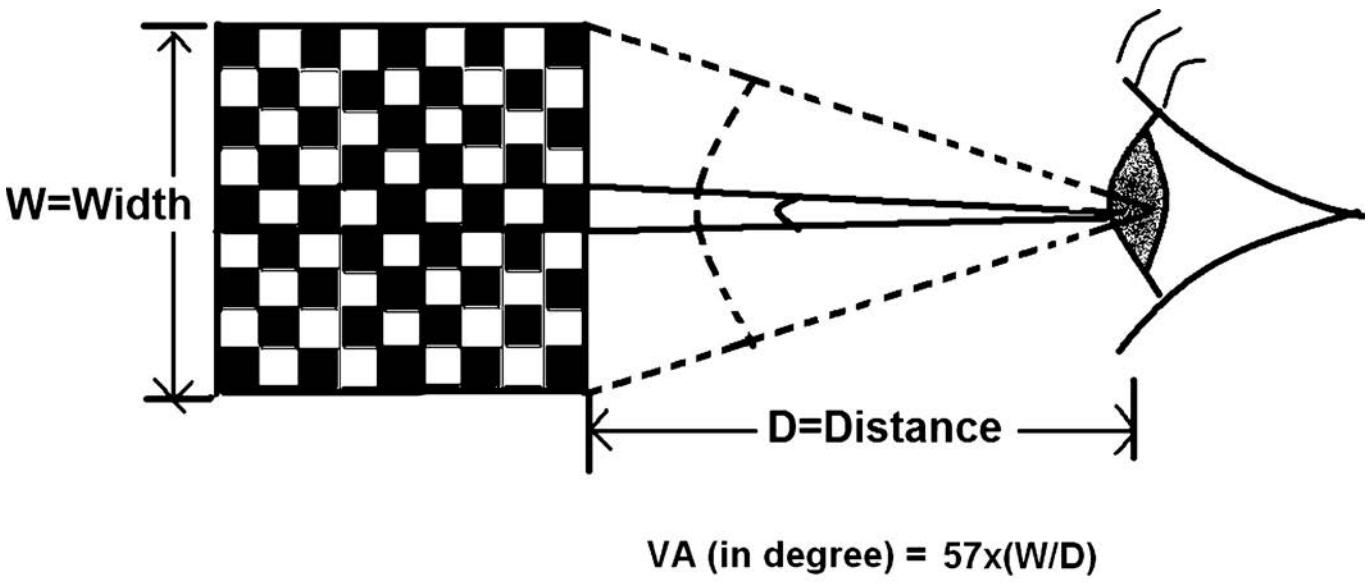
Visual angle (VA) is dependent on the distance from the subject's eyes to the screen and the width of the screen (see Fig. 2-2). This can be calculated by the following formula: visual angle = tangent (size of screen/distance) × 2. This is approximated by

the formula  $VA = 57.3 \times W/D$  ( $VA$  = visual angle,  $W$  = width of screen,  $D$  = distance from subject's eyes to screen). For example, if the screen width is 20 cm and the distance to the screen is 100 cm (1 m), visual angle is 11.5 degrees ( $57.3 \times 20/100 = 11.46$ ). If a visual angle of 10 degrees is desired, the distance should be 114.6 cm [ $D = 57.3 \times W/VA$ ,  $57.3 \times (20/10) = 114.6$ ]. Decreasing the visual angle reduces the P100 amplitude with little change in latency; the amplitude decreases exponentially relative to the decrease of visual angle with a steep decrease with a VA of less than 8 degrees. The overall pattern width, therefore, should be greater than 8 degrees. However, the greater part of the P100 is generated by the central 10 degrees of vision with only a small contribution from more peripheral vision<sup>8</sup>; therefore, increasing the visual angle greater than 10 degrees shows only a small increase of the P100 amplitude.

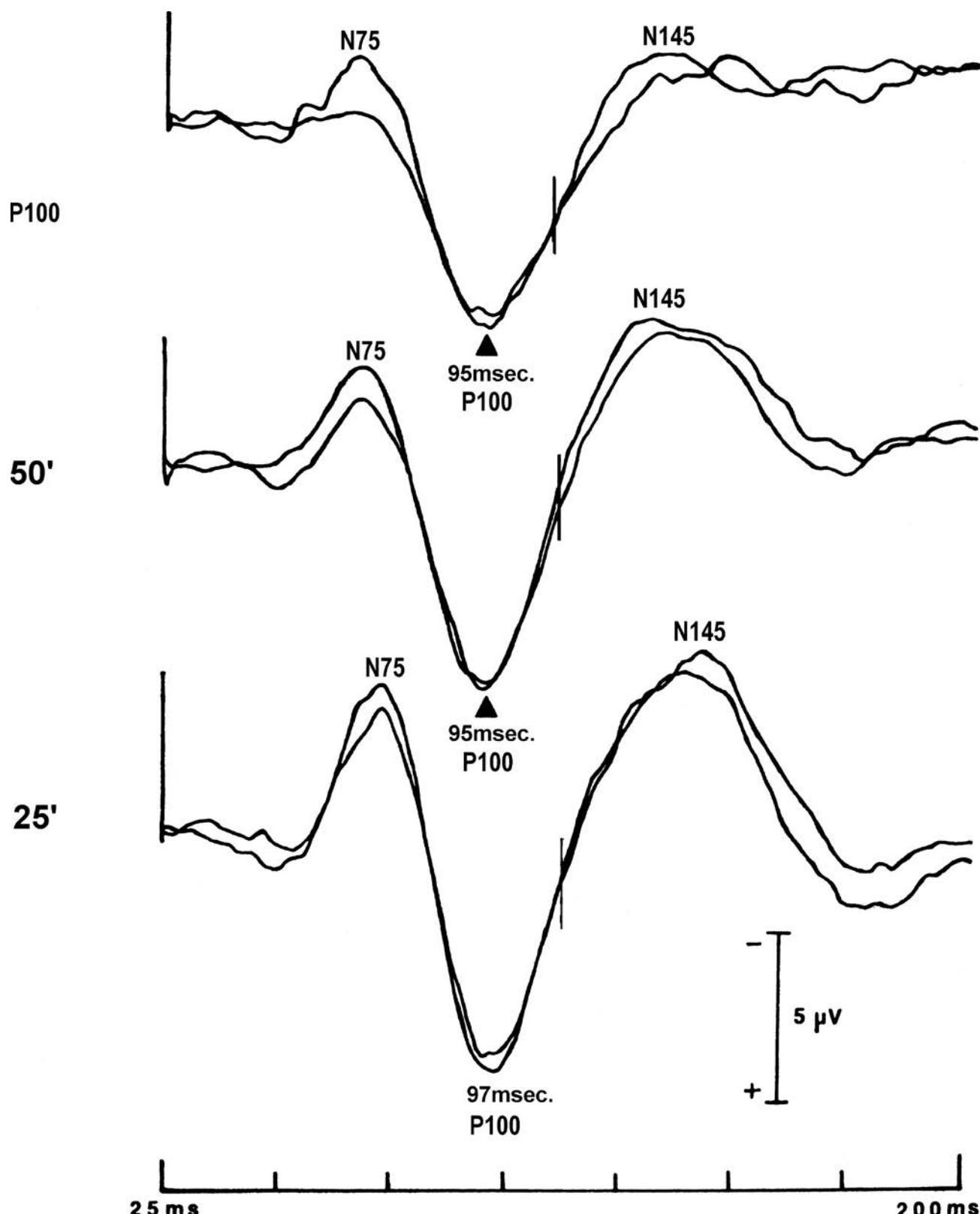
### CHECK SIZE

Check size is also dependent upon the width of the screen and distance from the subject's eye to the screen. The check size is expressed as the visual angle in minutes using the same formula as used for the screen size. Because one degree is equal to 60 minutes, the formula is approximated as  $VA = 60 \times 57.3 \times W/D$  or  $D = 60 \times 57.3 \times W/VA$ . ( $D = 3,438 \times W/VA$ ). In order to make a check size of 25' (minutes) with check size of 1 cm width on the screen, the distance should be 137.5 cm [ $3,438 \times (1/25) = 137.5$ ].

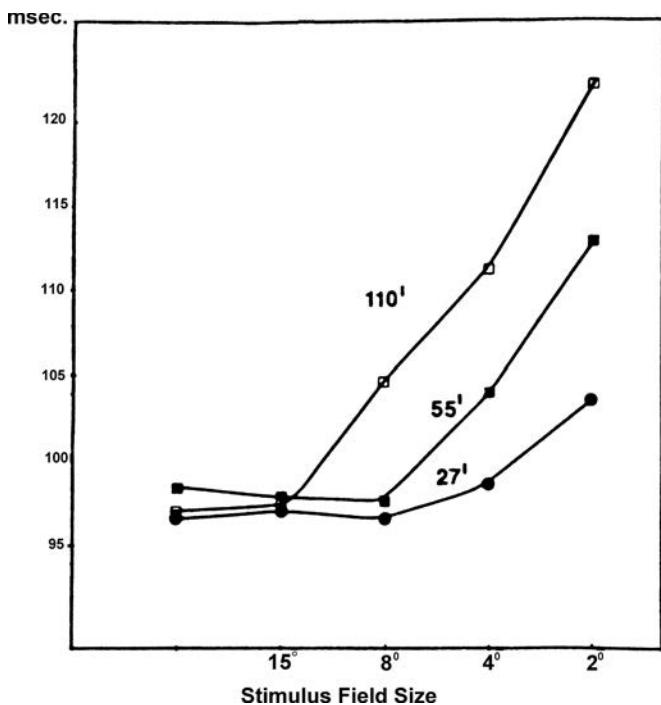
Generally a small check size (10'-20') evokes greater P100 amplitude (Fig. 2-3) but this differs depending on the field size; stimulation of the central 4 degrees of the field elicits maximum P100 amplitude by a small (27') check size, while a large field stimulation (32 degrees) evokes the largest amplitude with larger (55') check size.<sup>8</sup> The central 4 to 5 degrees of the retina (foveal vision) is most sensitive to small check size



**Figure 2-2.** Checkerboard pattern stimulation. The visual angle for check size (and screen size) is dependent on the width of check (or screen) and the distance to the eye.



**Figure 2-3.** Typical normal VEP to three different check sizes with a screen visual angle of 15 degrees. Note that the latency difference between three check sizes is minimal and the amplitude is highest using the smallest (25') check size. Small vertical lines indicate upper limit of normal latency. (From Oishi M, Yamada T, Dickins S, et al. Visual evoked potentials by different check sizes in patient with multiple sclerosis. *Neurology* 1985;35:1461-1465, with permission.)



**Figure 2-4.** P100 latency in relationship with stimulus field size and check size. Note: the latency is much greater with a larger check size (110') than a smaller check size (27') when the field size is small,<sup>20</sup> but the latency differences become much less with a larger (>15 degrees) field size. (From Yiannikas C, Walsh JC, McLeod JG. Visual evoked potentials in the detection of subclinical optic toxic effects secondary to ethambutol. *Arch Neurol* 1983;40:645–648, with permission.)

and generates a larger part of the VEP, whereas the peripheral part of retina reacts more to the larger check size.

The latency of P100 is affected by the check size and also the visual angle of the field, especially when the stimulus field size is small. If the field size is at or greater than 15 degrees, there is little latency difference between small (27'), medium (55'), and large (110') check sizes (Fig. 2-4). However, as the field size decreases, the large check size shows much longer P100 latency than the small check size. For example, P100 latency elicited by a large check size is more than 10 ms longer than that by the small check size when 4 degrees field size is used (Fig. 2-4).<sup>8</sup>

The most commonly used check size is about 20' to 25' since a smaller check size, in general, has greater sensitivity in revealing abnormalities. If the patient's visual acuity is too poor to distinguish the check, a larger check size may be used. P100 amplitude is largest with the smallest check if that size can be distinguished clearly; for example, with visual acuity of 20/25, 10' check size elicits the maximum amplitude, while 50' or greater check size can yield a response of normal latency but with decreased amplitude when visual acuity is 20/200 or less (see Fig. 2-11C).<sup>9</sup>

## LUMINANCE

The luminance of the screen has an effect on P100 latency and amplitude. P100 latency increases as the pattern luminance decreases.<sup>10,11</sup> Absolute luminance values are measured by a

photometer in units of candela/meter<sup>2</sup> (cd/cm<sup>2</sup>). The P100 latency increases linearly with the decrease of luminance. The latency increase is approximately 15 ms per log unit reduction in luminance, with a parallel reduction in amplitude of approximately 15% per log unit luminance reduction.<sup>10</sup> Once the luminance has been set, the brightness control should not be changed.

Pupillary diameter also has an effect on retinal illumination. Pupils constricted by pilocarpine will produce latency prolongation of several milliseconds.<sup>12,13</sup> However, the pupillary size has a less significant effect to patterned stimuli as compared to VEP elicited by diffuse light. Therefore, only when the patient has a gross difference in pupillary diameter between the two eyes should it be taken into account for interpretation.

Ambient light in the recording room should be kept dim so that this does not significantly affect the luminance of the stimulus. Again, it is important to stabilize the ambient light, once it is established.

## CONTRAST

The degree of contrast is determined by the formula  $(L_{\max} - L_{\min})/(L_{\max} + L_{\min})$  ( $L_{\max}$  is light and  $L_{\min}$  is dark luminance). Change in the degree of contrast between the black and white checks has little effect on the VEP as long as the contrast is clearly discernible. Extreme reduction of the contrast, however, causes increased latency and decreased amplitude of P100.<sup>14</sup> The change of luminance in sinusoidal grading pattern stimulation is gradual and follows the sine wave form.

## STIMULUS REPETITION RATE

The stimulus repetition rate of one to two pattern reversals per second (two pattern reversals equal to one black-white-black cycle) is appropriate, and faster stimulus rates will increase the P100 latency. The stimulus rate should not be faster than 4 to 6/s because the preceding response starts to overlap with the following response.

## REPLICATION

Measuring latency and amplitude of any evoked potential response is difficult if the response is contaminated by excessive "noise," especially when only a single tracing is available. Replication of the response is imperative to correctly identify and measure the latency and amplitude of the peaks of the response. At least two tracings should be superimposed for any evoked potential study. Superimposing three or more tracings is useful if the response is excessively "noisy". After verifying the response peak and trough from two or more superimposed tracings, a grand averaged tracing can be obtained by summing all responses.

## DEALING WITH "NOISY" RESPONSES

The most common source of "noise" is myogenic. Myogenic potentials can be minimized by instructing the patient to "open the mouth slightly and relax the jaw", and encourage the patient to decrease body movement or eye blinking during the test. High-frequency noise or 60-Hz artifacts from other electrical devices may be minimized by assuring low and balanced electrode

impedances. The video monitor screen (cathode ray) may generate 60-Hz artifacts especially when the subject is situated too close to the screen. Unlike other evoked potentials (brainstem auditory evoked potentials or somatosensory evoked potentials), the 60-Hz filter may be used if the artifact cannot be eliminated by other trouble-shooting methods. VEP frequency does not overlap with 60 Hz, and also 60-Hz ringing (see Fig. 1-14) does not occur in VEP recording. If the response remains "noisy" after completion of the averaging based on the protocol, do not hesitate to continue averaging and increase the number of summations, for example, from 200 to 300 repetitions. However, the patient may be tired of fixing a gaze during prolonged testing and may even doze off with partial or complete eyelid closure. Then the obtained result is unreliable. If the first response showed a well-defined normal response but repeated trial produced a low amplitude response with prolonged latency, it raises a possibility that the patient might have dozed off during the second procedure. It is important for the technologist to make sure that the patient is constantly focusing on the center of the screen and to encourage the patient to do so.

## PHYSIOLOGICAL FACTORS

### FULL FIELD VERSUS HALF FIELD AND MONOCULAR VERSUS BINOCULAR STIMULATION

The most commonly used stimulation method is full-field stimulation, which is the most sensitive in detecting lesions anterior to the optic chiasm. The subject is instructed to focus at the center of screen. If the patient is suspected to have half or partial visual field defect, half- or quarter-field stimulation may be used. Half-field stimulation is presented by blocking half of the checkerboard pattern, and the subject is asked to focus at about 0.5 to 1.0 degree outside the edge of the stimulus field. It may be difficult for some subjects to fix the gaze outside the checkerboard pattern when patterns are moving because it is a natural tendency to shift the gaze toward the moving object (checkerboard field). The technologist must make sure that the patient is gazing at the marked spot on the screen. The upper and lower fields or quarter-field stimulation can be accomplished in the same manner.

Most clinical studies use monocular stimulation and rarely use binocular stimulation. Binocular stimulation may be used for patients with homonymous visual field defects, which may produce asymmetric responses between LO and RO electrodes, similar to the hemifield stimulation (see Figs. 2-9 and 2-12).

### AGE

Most studies agree that there is no significant age-related P100 latency change until the fifth decade but thereafter a 2 to 5 ms latency prolongation per decade occurs.<sup>12,15,16</sup> Another study has shown a more linear increase of P100 latency along with age with greater prolongation with smaller checks and lower-intensity stimulation.<sup>17</sup> In clinical practice, the age factor is generally not considered if the normal data includes subjects of each decade age (10–70 years). For detailed research studies, however, age-dependent normal data must be used.

Testing VEP in young children or neonates is difficult because of lack of cooperation. LED goggle stimulation is often used. In neonates, successful recording using pattern shift

stimulation showed that P100 latency decreases rapidly during the first year of life and reaches adult values by the end of the first year. P100 latency may reach adult levels by 5 months of age when a medium check size (30'–50') is used, whereas the latency does not reach adult values until 5 to 6 years with the smaller check (12'–15').<sup>18</sup>

### VISUAL ACUITY

Decreased visual acuity diminishes the P100 amplitude but is less sensitive in latency changes. Small checks evoke the maximum amplitude response when the best corrective lens is used. If the patient has decreased visual acuity, P100 amplitude to small check size would be smaller than the larger check size. Generally the latency is affected little by decreased visual acuity if a large enough check size is used; even 20/200 visual acuity may show a normal P100 latency if medium (50') or large (100') check size is used.

### GENDER

In one study, P100 latency was found to be a few milliseconds shorter in females than in males, presumably due to a smaller head size or higher body temperature in females,<sup>12</sup> while others<sup>19</sup> did not find significant gender differences. Because the gender difference, if any, is minute (probably within the range of measurement error), gender is generally ignored in assessing abnormality clinically.

### BODY TEMPERATURE

Raising body temperature in normal subjects does not produce significant changes in P100 latency.<sup>20,21</sup> The increased body temperature tends to worsen the symptoms of multiple sclerosis (MS), but reports concerning a rise in body temperature in MS patients have been conflicting.<sup>21,22</sup>

### PUPILLARY SIZE

Normally, pupillary size has little effect on pattern reversal VEP, but extreme miosis (small pupil) or mydriasis (large pupil) may affect the latency and amplitude.

## AMPLIFIER AND SIGNAL AVERAGER SETTINGS

Since VEP has a relatively larger signal (5–10 µV) than other EPs, less amplification is required, generally a gain of 20,000 to 50,000. The low filter (LF) is 1 to 3 Hz and the high filter (HF) is 100 to 300 Hz. Besides a filter's effect on amplitude, latency will be shorter with increased low filtering (higher number of low filter setting) or with decreased high filtering (higher number of high filter setting) (see Fig. 1-13). The sweep time (analysis time) is 200 to 300 ms but longer sweep times may be used if P100 is markedly prolonged. A minimum of 2 ms of dwell time (sampling rate) is recommended for acceptable VEP waveform resolution. The number of sample summations is at least 100, but may be increased to 200 or more if the response is "noisy" or of low amplitude.

## RECORDING ELECTRODES

The most commonly used electrode placement for VEP is the *Queen's Square System* (this name comes from Dr. Halliday's laboratory at Queen's Square Hospital in London). The electrodes used are labelled as LO (left occipital), MO (mid-occipital), RO (right occipital), and MF (mid-frontal). MO is placed at the midline 5 cm above the inion, LO and RO are 5 cm lateral to the left and right of MO, respectively, and MF is at the midline 12 cm above the nasion (Fig. 2-5).

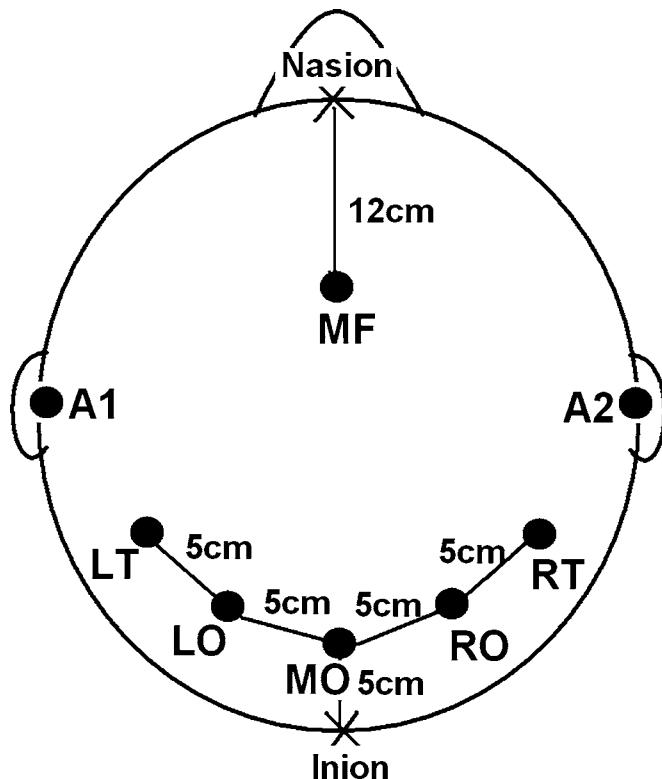
The following montage is recommended by the American Clinical Neurophysiology Society (ACNS)<sup>23</sup> for a four-channel recording utilizing full-field stimulation. (see Fig. 2-6).

- Channel 1: LO – MF
- Channel 2: MO – MF
- Channel 3: RO – MF
- Channel 4: MF – A1 (A2 or A1 + A2)

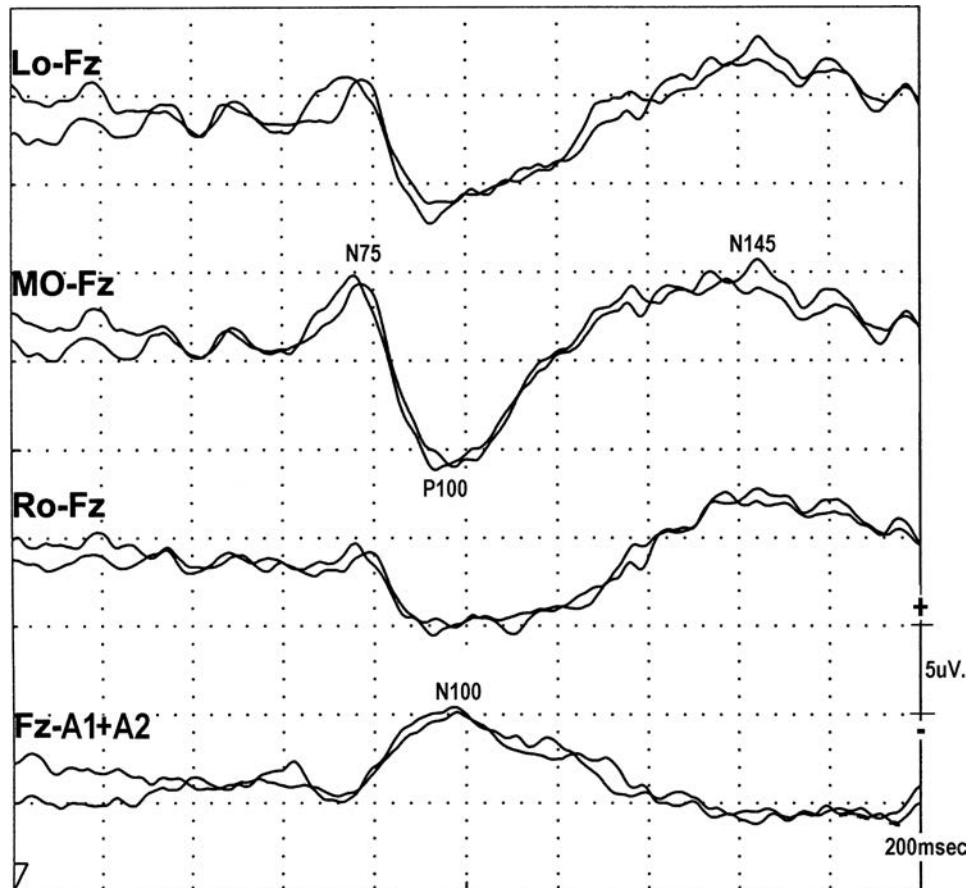
## NORMAL VEP IN FULL-FIELD MONOCULAR STIMULATION

### NORMAL WAVEFORMS AND DISTRIBUTION

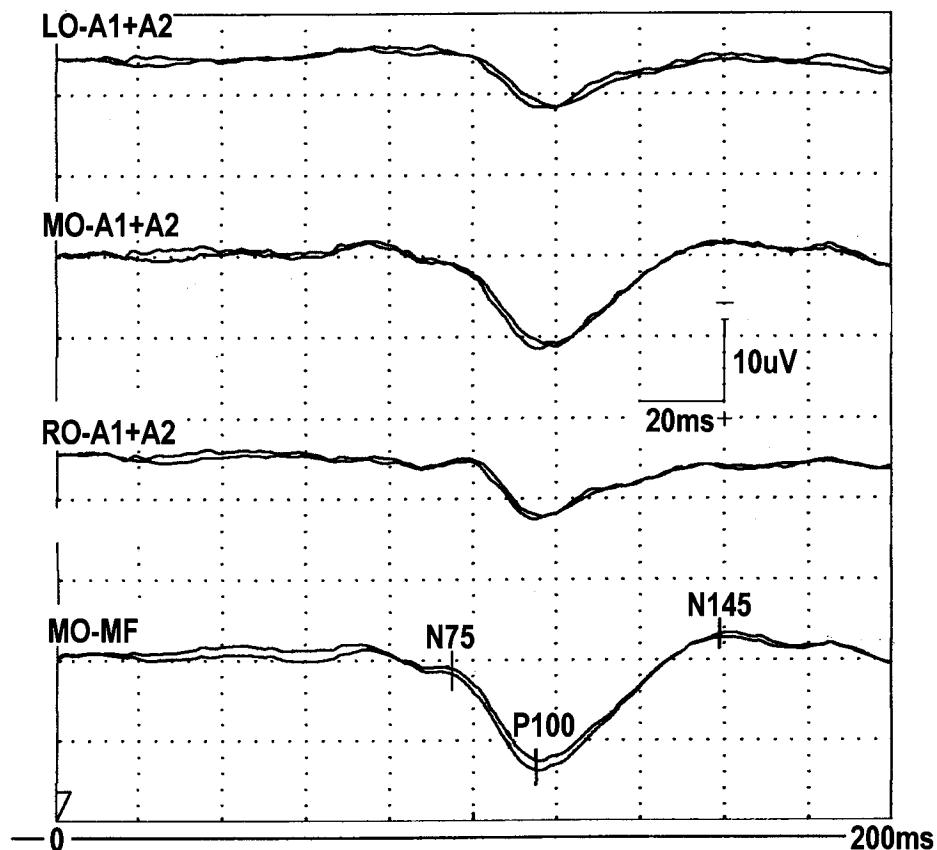
The waveform consists of initial negative (N75) followed by large positive (P100) and subsequent negative (N145) waves (Fig. 2-6). Of these, P100 is the most prominent and consistent. The amplitude is usually maximal at the MO electrode.



**Figure 2-5.** Queen's Square electrode placement system commonly used for VEPs.



**Figure 2-6.** Typical normal VEP to monocular stimulation. The waveform consists of an initial, relatively small negative potential (N75) followed by a large positive potential (P100), followed by a broad negative potential (N145). Of these, P100 is usually the most prominent and consistent potential. P100 amplitude is usually largest at the MO electrode. Because of the contribution of the negative potential (N100) at the MF electrode, MO-MF shows a larger potential than MO-ear reference recording. Note the symmetric response at RO and LO electrodes.



**Figure 2-7.** An example of alternative montage using ear reference.

The response at LO and RO are typically symmetric. From the MF electrode with an ear reference, a negative wave with a latency of 100 ms (N100) is recorded. Because of this polarity difference between the occipital (P100) and frontal (N100) electrodes, the MO-MF derivation usually shows a higher amplitude response than that recorded from MO with an ear reference (Fig. 2-7). Also the MO-MF response usually shows a “cleaner” response than the MO-ear reference response because the MF electrode is more free from muscle artifact than the ear reference (Fig. 2-7). If P100 latency is different between MO-MF and MO-ear recording, P100 from MO-ear recording should be chosen as P100. If the P100 amplitude or waveform is grossly asymmetric between LO and RO, hemifield or partial-field stimulation is required to verify the significance of the asymmetric response (see Fig. 2-12). This may imply a visual field defect.

#### NORMAL VARIATIONS

The initial negative peak (N75) may be small or may not be identifiable in some normal subjects, or N75 could be unusually prominent. When P100 is of very low amplitude, the location of the maximum amplitude of P100 may be displaced rostrally or caudally from the MO. In this case, additional electrodes may be necessary for appropriate measurement of P100.

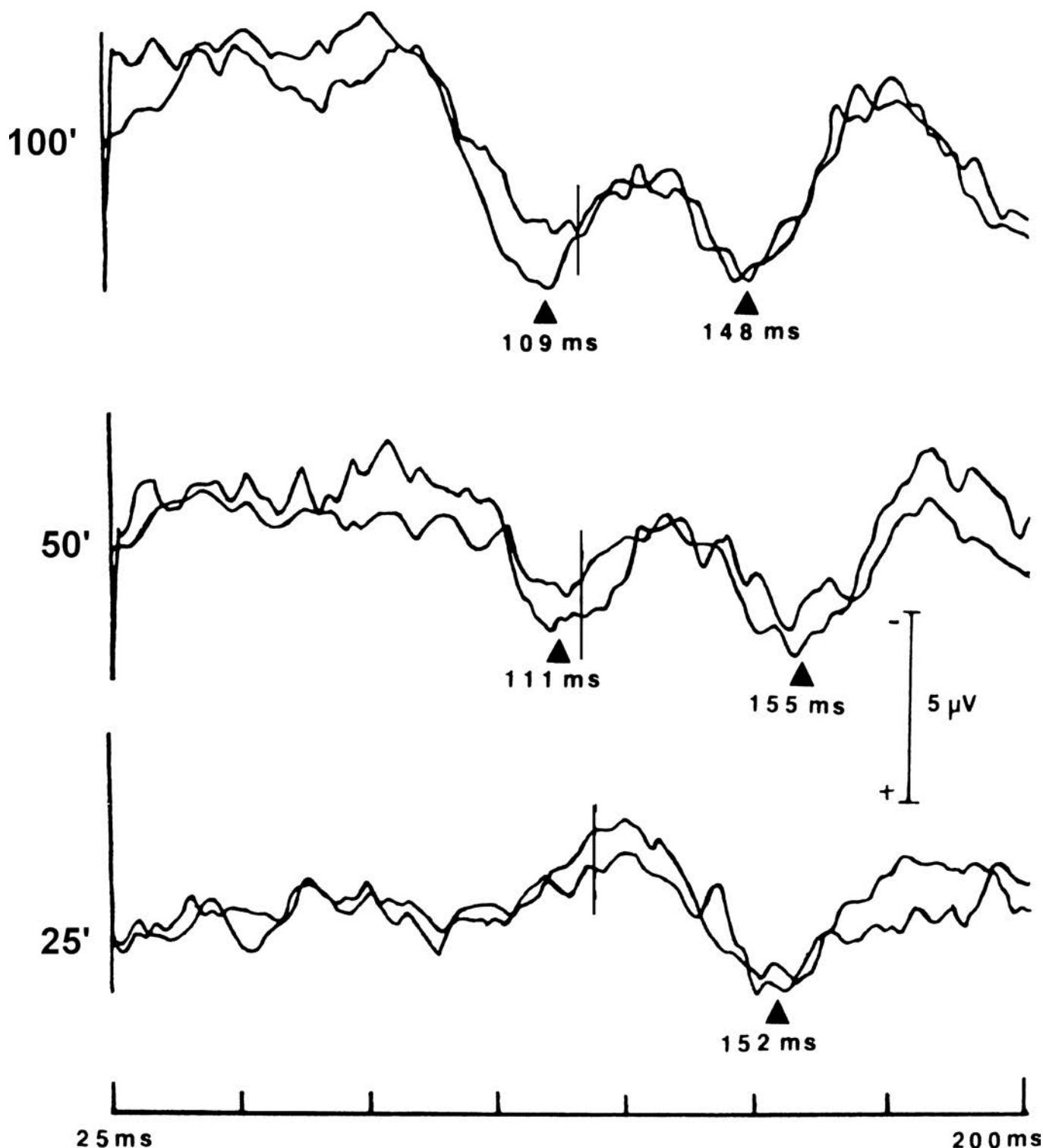
The most troublesome waveform variation is the “W” or bifid pattern (Fig. 2-8). The following conditions may contribute to a “W” shaped P100.

1. N100 from the MF electrode may have a different latency from that of P100 of the MO electrode, causing the waveform from the MO-MF derivation to have a bifid peak. This may be due to a contribution from the upper half field which generates N100 having a different latency from P100 latency (P100 is usually generated more by the lower than upper half-field stimulation).<sup>24,25</sup>
2. A bifid peak may appear only in response to a certain check size but not to other check sizes.<sup>26</sup> Examining other check sizes and finding the corresponding peak to one of the bifid peaks may be helpful in deciding which one of the bifid peaks is the “true” P100 (Fig. 2-8).
3. The response to full-field stimulation is the algebraic sum of activities generated by the nasal and temporal half fields’ stimulation. If there are latency differences between nasal and temporal half-field stimulation, this will result in a bifid P100 to full-field stimulation. In this case, examining nasal and temporal half-field stimulation is necessary.

#### HALF-FIELD STIMULATION

##### METHOD

If there is a gross asymmetry between LO and RO responses or anomalous wave forms by full-field stimulation, half-field stimulation may be performed to clarify the anomalous or ambiguous VEP. Half-field stimulation is more sensitive in detecting a chiasmal or postchiasmal lesion.



**Figure 2-8.** An example of "W" formed VEP in a patient with multiple sclerosis. Two positive peaks are identified with check sizes of 100' and 50'. The latency of the first positive potential is within normal limits, but the second potential is outside the normal limits (vertical lines indicate upper limit of normal latency), either with 100' or 50' check size. Using a 25' check size yielded a single positive potential with abnormally prolonged latency, which closely corresponded with the second positive peak of the 50' and 100' check sizes. Based on this finding, it is reasonable to conclude that the "true" P100 is the second positive peak in the 50' and 100' check sizes. (From Oishi M, Yamada T, Dickins S, et al. Visual evoked potentials by different check sizes in patient with multiple sclerosis. *Neurology* 1985;35:1461–1465, with permission.)

The fixation point is about one check-width lateral to the edge of half-field stimulation on the side of blank screen. Half-field stimulation requires much greater cooperation of the patient than full-field stimulation because it is difficult to fixate the gaze to a blank screen when the other half of the screen shows alternating movement of black and white checker patterns. In order to stimulate left and right visual fields in the same time domain, newer stimulus devices can deliver left and right alternating half-field stimulation.

In order to optimally visualize the response from ipsi- and contralateral sides, the ACNS<sup>23</sup> recommends the following montage.

For left half-field stimulation

Channel 1: LO - MF  
Channel 2: MO - MF  
Channel 3: RO - MF  
Channel 4: RT - MF

For right half-field stimulation

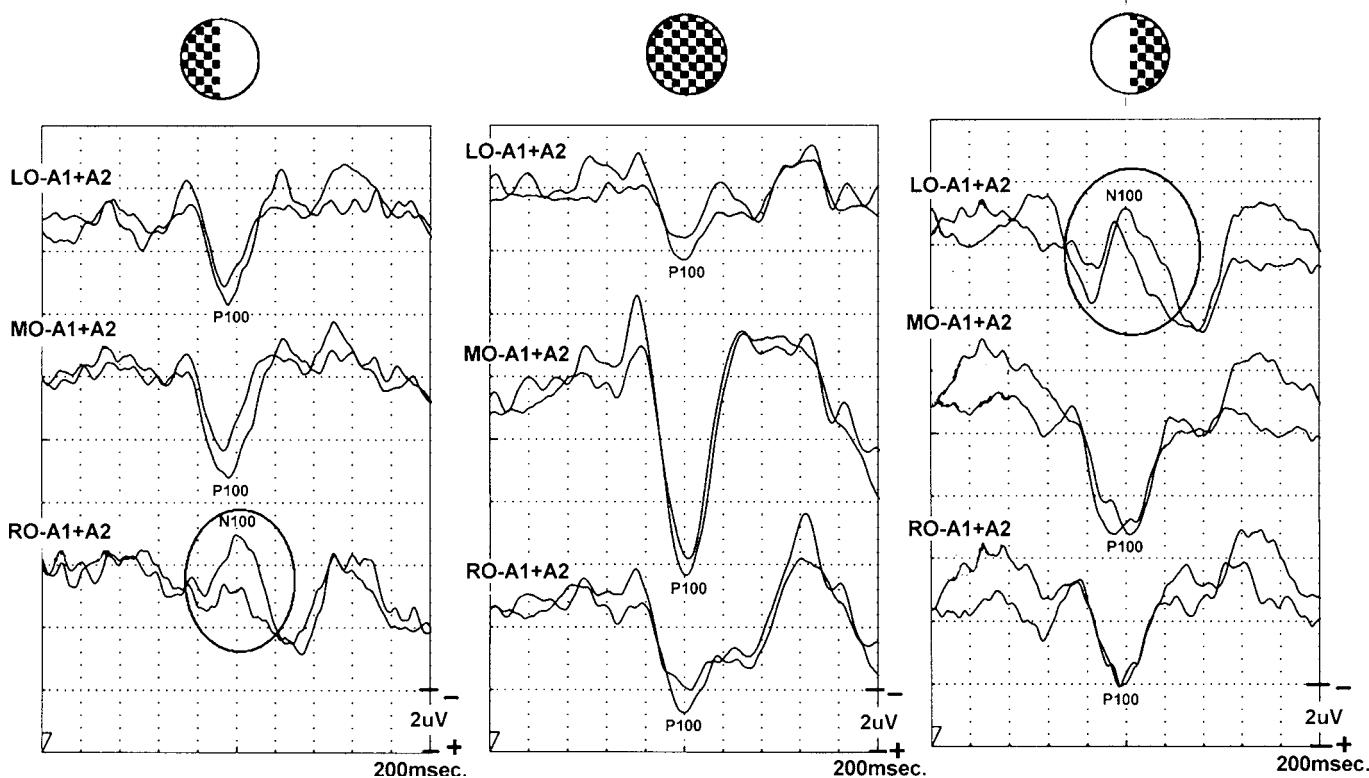
Channel 1: LT - MF  
Channel 2: LO - MF  
Channel 3: MO - MF  
Channel 4: RO - MF

(LO, left occipital; RO, right occipital; LT, left posterior temporal; RT, right posterior temporal; MF, midfrontal.)

### NORMAL VEP TO HALF-FIELD STIMULATION: "PARADOXICAL LATERALIZATION"

The visual input from the left visual field activates the right visual cortex and vice versa. Hemifield stimulation, therefore, is expected to yield a larger amplitude response on the occipital cortex contralateral to the side of stimulated visual field. Contrary to this expectation, the VEP amplitude is greater at the ipsilateral than the contralateral occipital electrode in (Fig. 2-9).

This anatomically contradictory phenomenon is called "paradoxical lateralization."<sup>27</sup> A small check size preferentially activates the central retina, which projects to the occipital pole, whereas a large check size activates the more peripheral retina which projects to the more deeper medial surface of the occipital cortex (see Fig. 2-1). Activation of the medial surface using a large check size creates a vector projecting more to the contralateral electrode than to the ipsilateral electrode (see Fig. 2-1). Therefore, the paradoxical lateralization is more prominent when large check size (>50 degrees) is used.<sup>28,29</sup> Similar paradoxical lateralization can be observed in somatosensory evoked potentials of the lower extremity nerves. Like the activation of the medial occipital cortex of the visual system, distal peripheral nerves of the lower extremity, such as the tibial nerve at the ankle, project to the medial surface of the parasagittal cortex (see Fig. 4-22).



**Figure 2-9.** VEP waveform and distribution of half-field stimulation. The signal from a large check size (100 minutes) is received in the medial aspect of the occipital lobe. The vector of this input activity is directed more toward the ipsilateral than the contralateral hemisphere (in relation to the side of the stimulated half field) (see Fig. 2-1). This results in a larger amplitude P100 on the side ipsilateral to the stimulated field (paradoxical lateralization). Note the larger amplitude of P100 at the LO electrode to the left half-field stimulation and vice versa. There is a negative potential (shown by circle) which shows near-phase-reversal relationship with P100 at the contralateral- or mid-occipital electrode.

Hemifield VEP, best recorded at the lateral occipital or posterior temporal electrode, consists of N75, P100, and N145, similar to the MO response. The response on the contralateral occipital or posterior temporal electrode shows a nearly phase-reversed relationship with the ipsilateral VEP, consisting of P75, N105, and P135 (see Fig. 2-9). However, the paradoxical lateralization by half-field stimulation is not a consistent finding presumably due to considerable inter-individual anatomical variation in the cortical representation of the occipital lobe.

## ABNORMAL VEP

VEP to full-field stimulation is usually maximal at the midoccipital electrode, where N75, P100, and N145 components are best identified. Also, N100 from the midfrontal electrode may be measured. Of these components, P100 is the most consistent and reliable potential for VEP assessment. The following parameters are measured.

1. Absolute latency of P100 at MO from left (OS) and right (OD) eyes.
2. Latency difference of P100 between OS and OD (interocular latency difference).
3. Amplitude of P100 at MO and its difference between OS and OD (interocular amplitude difference).
4. Amplitude ratio of P100 between LO and RO electrodes (interhemispheric amplitude ratio).

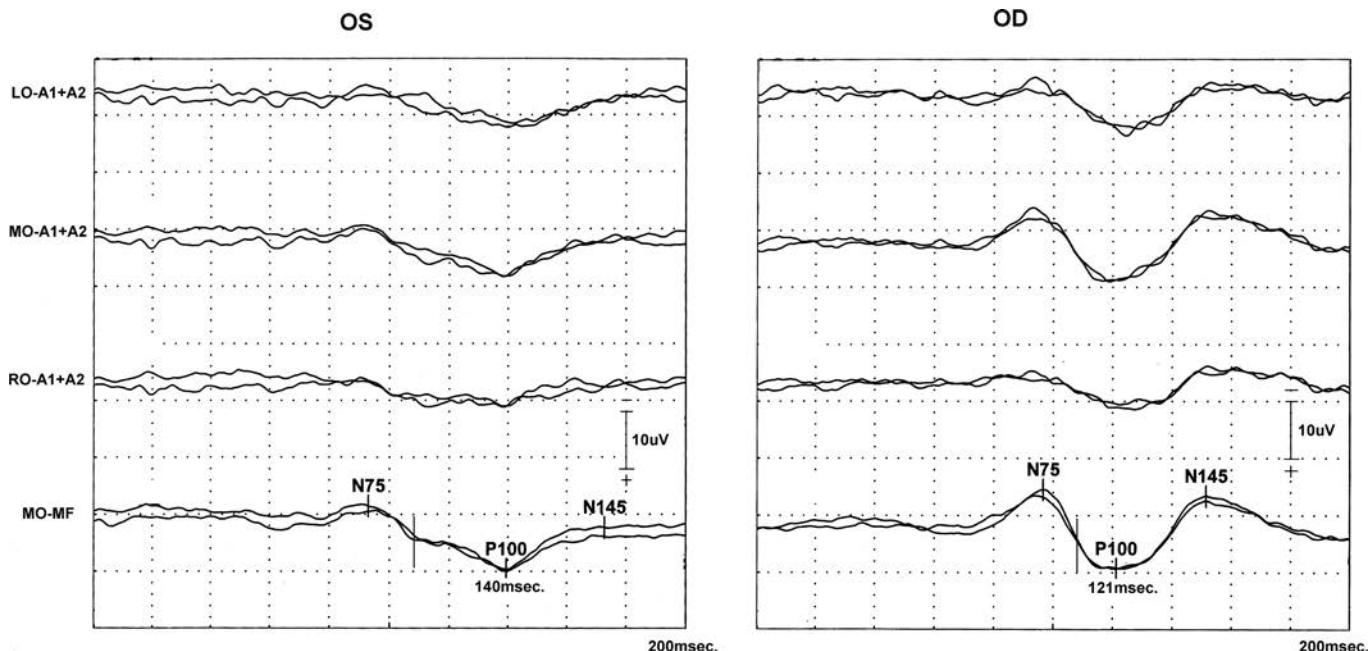
VEP abnormalities may occur from dysfunction in any part of the visual system, including ocular and retinal disorders. Only when ocular and retinal disorders are excluded are VEP abnormalities an indication of central visual pathway dysfunction. Monocular abnormalities indicate a unilateral optic nerve dysfunction, assuming that retinal or ocular abnormalities are excluded. When VEPs are abnormal in both eyes (binocular abnormalities), it is not possible to differentiate pre-and

postchiasmatic lesions. In this case, further evaluation of hemifield stimulation may be examined.

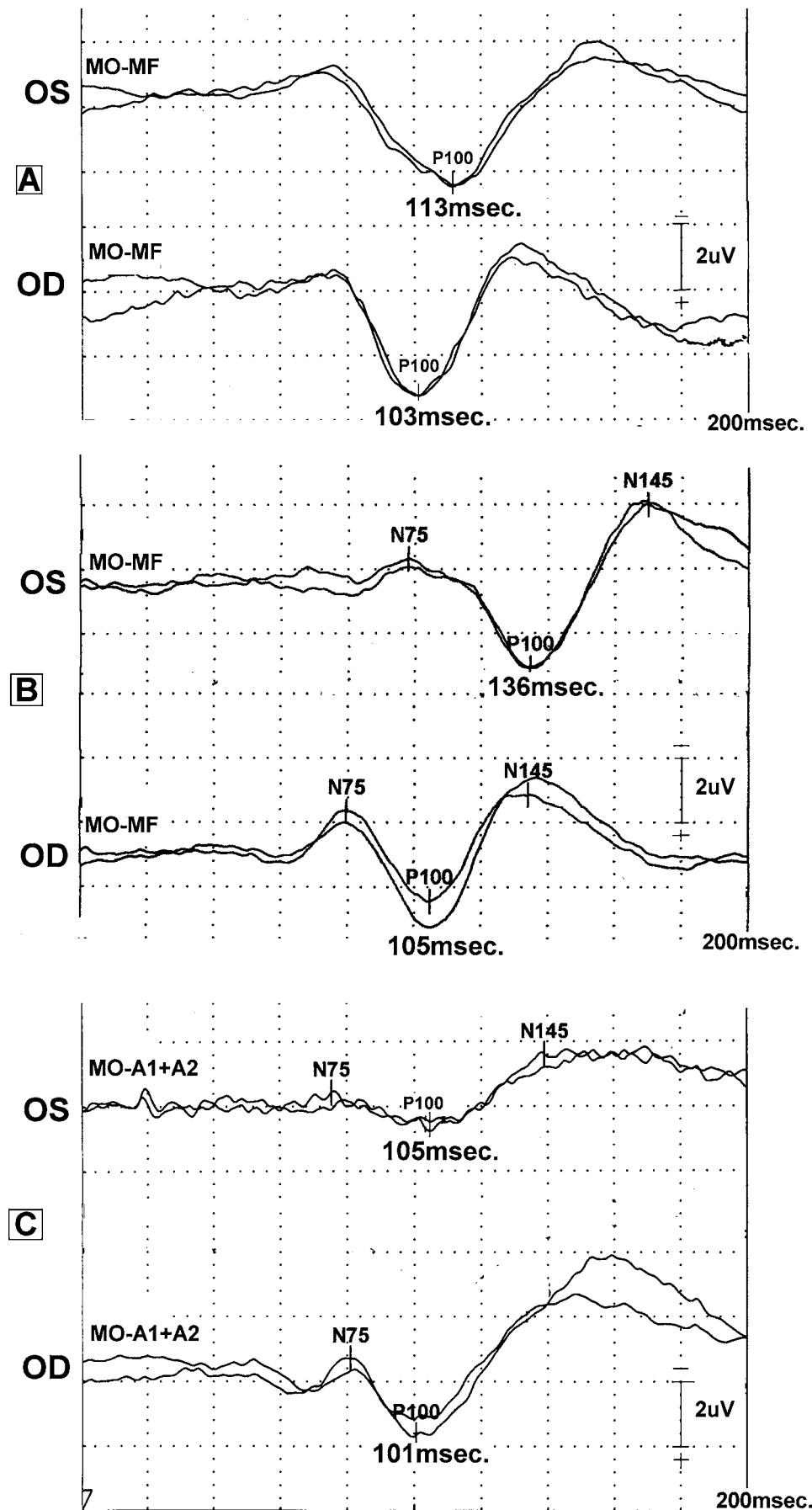
## LATENCY ABNORMALITIES

The P100 latency measurement is the most sensitive and reliable indicator in determining VEP abnormalities. N75 and N145 components have excessive variations in latency and amplitude, thus they are not included for abnormal criterion. As discussed previously, P100 latency varies depending on the testing conditions, but most laboratories agree that the upper limit of normal is around 115 to 120 ms which is 2.5 to 3 SD above the normal mean values (Figs. 1-18 and 2-10). (Table 2-1) The latency difference between the two eyes (interocular latency difference) is in some cases more sensitive than the absolute latency. The upper limit of normal for interocular difference is usually 6 to 8 ms (Table 2-1). In measuring latency, 1 to 2 ms can be within the range of measurement error or variation. If interocular latency difference is at or greater than 10 ms this is definitely abnormal (Fig. 2-11A). One should be conservative in determining abnormality when measured latency is close to the upper limit of normal. When repeated trials show considerable latency differences, the shortest latency peak with the most well-formed response should be picked as P100. When there is a small latency difference between the two trials, a mean or grand averaged response of two trials is accepted as P100 peak latency.

The latency is most sensitively affected by demyelinating diseases, with relatively well-preserved amplitude and waveforms (Fig. 2-11A,B). This is in contrast to axonal damage that affects the amplitude more than the latency (Fig. 2-11C). Compressive lesions tend to depress amplitude at first and prolong the latency when it becomes severe. A significant increase of P100 latency to one eye only or a great difference in interocular latency (even if both are prolonged) most likely indicates a prechiasmatic lesion (see Fig 2-11B).



**Figure 2-10.** An example of abnormal VEP with prolonged P100 on both eyes. Vertical lines indicate upper limit of normal latency.



**Figure 2-11.** Abnormal examples of VEPs shown in three patients. In patient A, absolute latencies of both OS and OD were within normal limits, but the latency difference between the two eyes (interocular latency difference) was 10 ms, which is more than the allowable difference ( $>3$  SD). In patient B, OD had a normal P100 latency, but OS showed a significantly delayed P100. In subject C, the latencies of both eyes were within normal limits, but the amplitude was much smaller on OS than on OD. The amplitude difference was due to decreased visual acuity in OS (20/200) compared to that of OD (20/20).

<b>TABLE 2.1</b>		VEP Normal Values		
Absolute	25 min	50 min	100 min	
Mean	97.2	97.7	100.3	
SD	4.5	3.7	3.6	
Upper limit	110.7	108.8	111.1	
<i>L-R Difference</i>	25 min	50 min	100 min	
Mean (ms)	1.8	1.3	1.5	
SD	1.4	1.0	0.9	
Upper limit	6.0	4.3	4.2	

The above values are in milliseconds.

### AMPLITUDE ABNORMALITIES

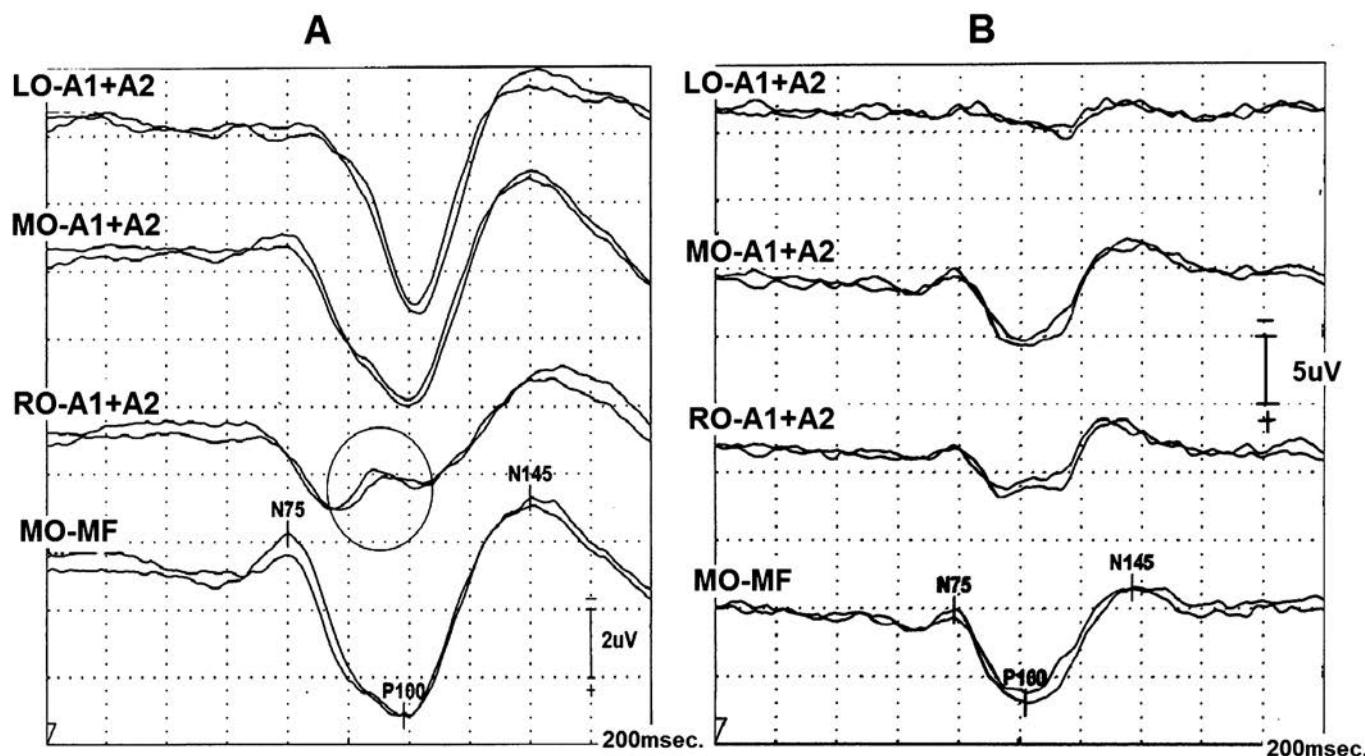
The amplitude varies considerably between subjects and also between two eyes within one subject. Since amplitude as well as interocular amplitude ratios do not follow the normal (Gaussian) distribution, mean plus standard derivation cannot be used for abnormal criteria. The most reliable amplitude abnormality is the total absence of response or exceedingly low amplitude response in one eye or both eyes. In this case, the analysis time may be increased to 300 ms or greater to exclude the possibility that the P100 latency is extremely prolonged beyond the routine time scale of 200 to 300 ms.

In the case of low-amplitude VEP, especially in both eyes, it may be necessary to examine the response at the anterior, posterior, or lateral electrodes because the maximum P100 amplitude may not necessarily be at the MO electrode. If, however, the amplitude in one eye is depressed greater than 50% to 75% as compared to the other eye, this can be considered to be abnormal (see Fig. 2-11C).

P100 amplitude also correlates with visual acuity, and any condition that impairs visual acuity will decrease the amplitude. Therefore, VEP should be tested with the best corrected vision if the patient wears glasses. Technical factors such as poor fixation, defocusing, nystagmus, or drowsiness can cause the amplitude reduction.

### TOPOGRAPHIC ABNORMALITIES

A mild degree of amplitude asymmetry between left and right laterally placed electrodes (LO and RO) to full-field monocular stimulation is not uncommon in normal subjects. However, if the amplitude asymmetry is greater than 50% or there is a significant difference in waveforms between LO and RO responses (Fig. 2-12), it is necessary to perform hemi- or partial-field stimulation to determine the significance of the asymmetry. For example, depressed LO response to both left and right monocular stimulation raises the possibility of a postchiasmal lesion in the right hemisphere (due to paradoxical lateralization). In this case, the depressed or absent response to the left hemifield



**Figure 2-12.** Examples of asymmetric VEPs between LO and RO electrodes to full-field left monocular stimulation. Note the depressed amplitude with a negative “bump” in the vicinity of P100 at RO in patient A. These features resemble half-field stimulation (see Fig. 2-9). In subject B, the amplitude was much depressed at LO compared to RO. These asymmetries suggest a possible visual field defect; the abnormality is at the left occipital lobe in patient A and right occipital lobe in patient B, suggesting a right and left visual field defect, respectively. Whether or not these asymmetric VEP features truly represent a visual field defect must be verified by half-field stimulation.

stimulation confirms the abnormality. If the abnormality by hemifield stimulation is limited to one eye, this suggests a prechiasmal dysfunction.

### WAVEFORM ABNORMALITIES

The morphological deviation of the VEP waveform, such as loss of N75 or N145, should not be considered abnormal in the presence of normal P100 latency and amplitude. The most confusing waveform is a double peaked or "W"-shaped P100. It is difficult to determine if the first or second peak is P100 or if neither or both are P100. There are a few possibilities to account for a "W"-shaped P100. P100 is primarily generated by the central visual field.<sup>29</sup> If the patient has a central scotoma, the VEP may show a negative instead of a positive peak at the midline due to the removal of the central visual field input. This would result in a "W"-formed P100 by partial contribution of positivity by surviving central vision and negativity by peripheral vision. In this case, laterally placed electrodes may show a "true" P100. The bifid P100 may also occur when the upper visual field contributes negative activity that may be shifted in latency relative to the P100 positivity. In this case, the lower half-field stimulation delineates a "true" P100. In some cases, different check sizes solve the problem as shown in Figure 2-8. One or two check sizes may show bifid P100, but one additional check may show a well-defined single peak. In this case, the peak that corresponds to the single-peaked P100 should be chosen as P100. Another possibility of a "W" waveform results from a contribution of N100 from the MF electrode which has a different latency from that of the occipital P100. In this case, P100 should be measured from MO with an ear reference derivation.

### VEP AND CLINICAL CORRELATES

VEP examines the integration of visual pathway including the cornea, retina, optic nerve, optic tract, lateral geniculate body, optic radiation, and occipital cortex (see Fig. 2-1). An abnormal VEP may be found in lesions along any of these anatomical structures. In general, the sensitivity is higher in lesions involving the optic nerve, especially when secondary to a demyelinating disease. Despite a high sensitivity of VEP abnormalities in optic neuritis and MS, the abnormalities are not etiologically specific.

### OPTIC NEURITIS

Following pioneering work by Halliday et al.,<sup>2</sup> a number of studies have agreed that the incidence of VEP abnormalities is close to 90% in patients who have a history of optic neuritis.<sup>10,19,30-33</sup> The VEP abnormality is characterized by a prolonged P100 latency. Since the abnormality is most commonly monocular, interocular latency difference is probably the most sensitive measure indicative of optic nerve dysfunction (see Fig. 2-11A,B). If both eyes are affected, degrees of P100 latency prolongation may be considerably different. Unlike axonal optic nerve pathology, the amplitude and waveform of P100 are often well preserved, which is characteristic for a demyelinating process. Complete absence of the VEP is rare except in patients with an acute state or severely impaired vision.

Since VEP abnormalities tend to persist after the clinical symptoms of optic neuritis disappear, abnormal VEP is useful to confirm a past history of optic neuritis. The VEP sensitivity is overall higher than MRI in detecting optic nerve lesions. This is especially true in asymptomatic patients who show MRI abnormalities only in 20%.<sup>34</sup> Optic neuritis is a risk factor for MS because many patients with optic neuritis eventually develop MS.<sup>35</sup>

### MULTIPLE SCLEROSIS

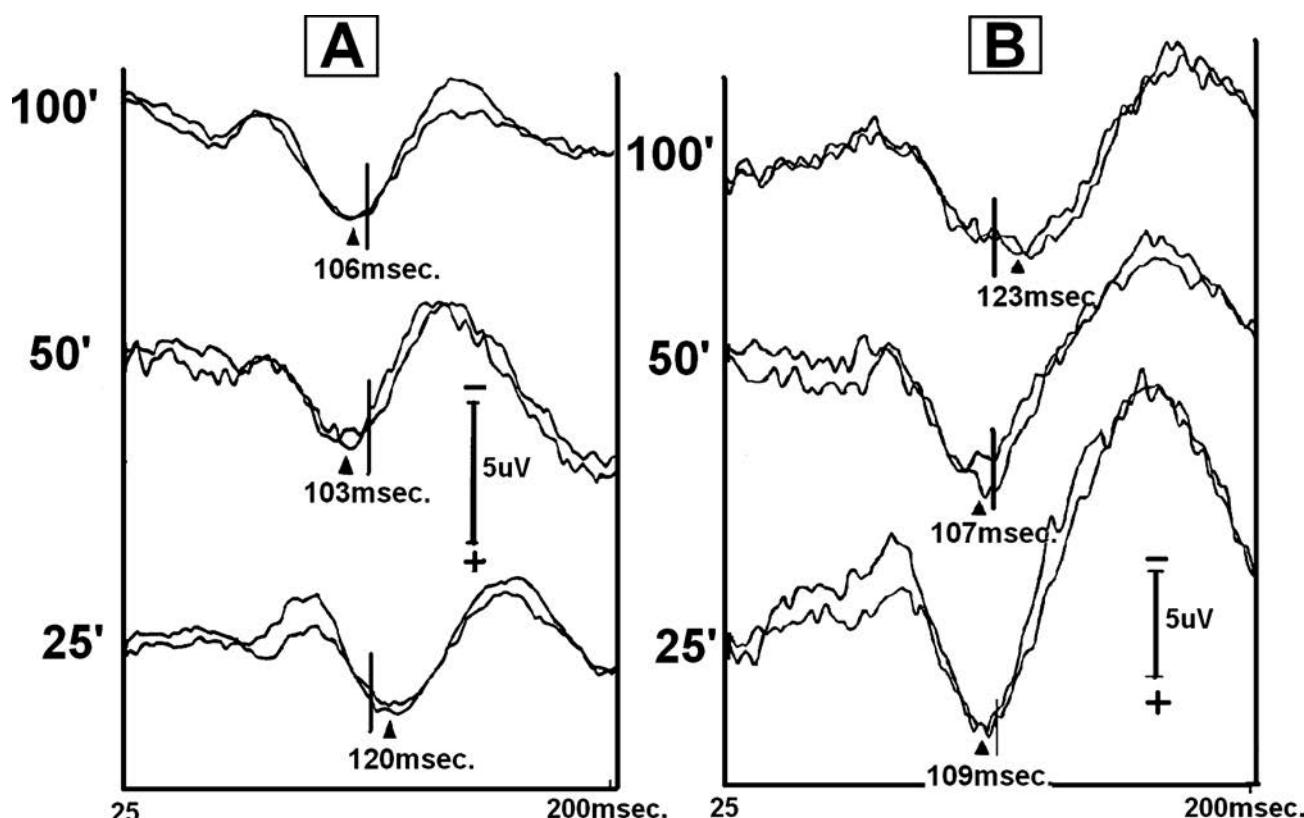
Optic nerve demyelination, which runs parallel with a high incidence of VEP abnormalities, is common in multiple sclerosis (MS) patients. VEP may be abnormal in MS patients who have no present or past history of visual symptoms. The abnormal VEP demonstrating a clinically "silent" optic nerve lesion raises the diagnostic possibility of MS in patients who have no visual symptoms but who have signs of other CNS lesions. The abnormal incidence in MS as a whole is about 60%.<sup>17,33,34,36-38</sup> When the MS diagnosis is classified as possible, probable, or definite, the abnormal ratios are about 40%, 60%, or 80% to 90%, respectively. If there is clinical evidence of optic neuritis, the abnormal incidence is close to 90%.<sup>39</sup> Even without clinical evidence of optic nerve involvement, half of the MS patients are expected to have abnormal VEPs. Conversely, it is extremely rare to find abnormal neuro-ophthalmological examinations when the VEP is normal.<sup>39</sup> Although VEP abnormalities tend to remain following an acute episode of optic neuritis,<sup>40</sup> in some patients (5% to 15%) prolonged P100 latency may return to normal within months to a few years.<sup>41,42</sup>

VEP abnormalities in MS patients are characterized by latency prolongation, by either absolute or interocular latency difference (see Figs. 2-10 and 2-11). The amplitude and waveforms are often well preserved. Significant prolongation of P100 latency with well-preserved amplitude in patients who have normal or near-normal visual acuity strongly suggests a demyelinating process rather than axonal or compressed optic nerve lesions. The abnormal incidence is higher with the use of smaller check size (25' or smaller), but the abnormality may be limited to only a large check size (100') in some patients (Fig. 2-13).<sup>26</sup>

Alternative stimulus methods such as hemifield stimulation<sup>42</sup> or lower luminance stimuli<sup>43</sup> reported an increased incidence of abnormalities in MS patients.

### COMPRESSIVE OR AXONAL OPTIC NERVE LESIONS

Tumors compressing the optic nerve mainly affect the amplitude and waveform with relative preservation of latency (see Fig. 2-11C). A latency prolongation of more than 20 ms with well preserved amplitude, which is common in demyelinating optic nerve lesions, is rare in compressive lesions. Unlike an abnormal VEP revealing clinically "silent" lesions in MS patients, an abnormal VEP due to a compressive lesion is usually accompanied by visual symptoms such as decreased visual acuity, optic atrophy, or visual field defects<sup>44</sup> and/or abnormal ophthalmological defects. Papilledema due to increased intracranial pressure or pseudotumor cerebri usually does not produce an abnormal VEP until a severe degree of increased pressure occurs.<sup>45</sup>



**Figure 2-13.** Two examples of abnormality limited to one check size observed in patients with multiple sclerosis. In patient A, the abnormality was limited to the smallest (25') check size while in patient B, the abnormality was seen only with the largest (100') check size. Vertical lines indicate upper limit of normal value for each check size.

Ischemic optic neuropathy also affects the amplitude more than the latency. The latency may be prolonged but usually not as dramatically as in MS.<sup>46</sup>

#### SPINOCEREBELLAR DEGENERATION

Abnormal VEP is found in about two thirds of patients with Friedreich's ataxia.<sup>47-49</sup> The abnormality is usually bilateral with fairly symmetric prolongation of P100 latency. The amplitude is usually preserved but may be more affected than in MS patients, especially in patients with severe visual impairments.

In contrast to the high incidence of VEP abnormalities in Friedreich's ataxia, other types of spinocerebellar degeneration usually have normal VEPs; they include hereditary spastic paraparesis,<sup>50</sup> hereditary cerebellar ataxia,<sup>48</sup> hereditary spastic ataxia,<sup>51</sup> and olivopontocerebellar atrophy.<sup>49,52</sup>

#### CHARCOT-MARIE-TOOTH DISEASE

VEP is abnormal in some patients with this disease (7 of 17 patients in one study),<sup>53</sup> although the patients usually do not have clinical evidence of optic nerve involvement. The VEP abnormalities are not related to the clinical severity of the disease.

#### PARKINSON'S DISEASE

VEP abnormalities reported in patients with Parkinson's disease are based on the statistical difference between normal and patient

groups rather than on individual findings. Using a sinusoidal grating stimulation, P100 latency in the normal group was  $116 \pm 9$  ms but in a group of Parkinson patients, it was  $139 \pm 22$  ms.<sup>6</sup> The results after treatment with dopamine varied, but one study found a reduced abnormality based on decreased interocular latency differences.<sup>54</sup> The responsible site for the abnormality is thought to be the inner plexiform layer of the retina which shows decreased dopaminergic cells in Parkinson patients.

#### TRANSVERSE MYELITIS

VEP in acute transverse myelitis is usually normal. The incidence of abnormality increases in chronic progressive myelitis, ranging from 35%<sup>55</sup> to 76%.<sup>56</sup> The diagnosis of MS becomes highly likely if abnormal VEP is found in patients with clinical evidence of myelopathy.

#### CHIASMAL LESION

Pituitary tumor, craniopharyngioma, or tumor near the sella turcica compressing the optic chiasm produces bitemporal hemianopsia (see Fig. 2-1). Based on paradoxical lateralization, the monocular full-field stimulation may show an asymmetric response between the left and right occipital electrodes with a depressed response on the electrodes ipsilateral to the side of visual field defect. Monocular temporal half-field stimulation produces either depressed response or no response in all electrodes. Due to considerable variation of waveform distribution, however, VEPs are of limited value in detecting a chiasmal lesion.

## RETROCHIASMAL LESION

In evaluation of postchiasmal lesions, VEP recorded from laterally placed electrodes (LO/RO or LT/RT; see Fig. 2-5) to partial-field stimulation must be examined. Due to paradoxical lateralization, a depressed left occipital response, for example, to both left and right monocular full-field stimulation suggests a lesion in the right hemisphere associated with left homonymous hemianopsia. Since the asymmetric responses between LO and RO are relatively common in normal subjects, presumably due to anatomical variations of occipital cortex, this alone is not a reliable finding to predict postchiasmal lesions. The findings, even with the use of half-field stimulation may not always be accurate.<sup>57,58</sup> In a study of 50 patients with homonymous field defects confirmed by perimetry, 79% showed VEP abnormalities.<sup>59</sup>

In order to circumvent the technical difficulty of half-field stimulation, sequential stimulation presenting left and right half-field stimulation alternately may yield more reliable results.<sup>60,61</sup>

## ALBINISM

This is an interesting condition in which about 20% of nasal half field from each eye projects to the contralateral visual cortex, in contrast to the normal in whom nasal half field projects to the ipsilateral hemisphere (see Fig. 2-1). Therefore, the inputs from the temporal and some of the nasal visual fields from each eye reach the contralateral occipital cortex. Full-field monocular stimulation thus shows a similar VEP asymmetry as elicited by the half-field stimulation.<sup>62</sup>

## HUNTINGTON'S CHOREA

The characteristic VEP feature of Huntington's chorea is low P100 amplitude but with normal latency.<sup>63,64</sup> The low-amplitude VEP may be seen in asymptomatic offsprings or high-risk subjects. Interestingly, the low-voltage EEG and somatosensory evoked potentials are also characteristic features for Huntington's chorea.<sup>63,65</sup>

## CORTICAL BLINDNESS

VEP results in patients with cortical blindness have been inconsistent. In a patient with lesions at Brodmann's area 17 (primarily visual cortex) but sparing area 18 and 19 (association cortex), transient and steady-state VEPs were found to be normal.<sup>66</sup>

However, VEP was found to be abnormal when high-frequency spatial grating was used.<sup>67</sup> The results of VEP using flash stimulation have also been inconsistent.<sup>68-70</sup> Since some patients with cortical blindness may have normal VEPs, differentiating between functional (factitious, hysterical, or malingering) and organic visual loss may be difficult. In general, however, the presence of well-formed normal VEP in patients complaining of a severe degree of visual loss, for example, visual acuity of less than 20/120, strongly suggests a functional visual disturbance.<sup>71</sup>

## FUNCTIONAL BLINDNESS, HYSTERIA OR MALINGERING

The presence of well-defined normal VEP is incompatible with moderate-to-severe visual disturbance. In this case, a functional

disturbance or malingering problem is suspected. However, it should be noted that if the patient is capable of defocusing intentionally to avoid perceiving the stimulus or of converging the eyes during the test, this could produce prolonged or absent P100. Some subjects can produce voluntary nystagmus during delivery of the stimulus. This may produce diminished P100 amplitude but with normal latency.<sup>72</sup>

## ELECTRORETINOGRAM

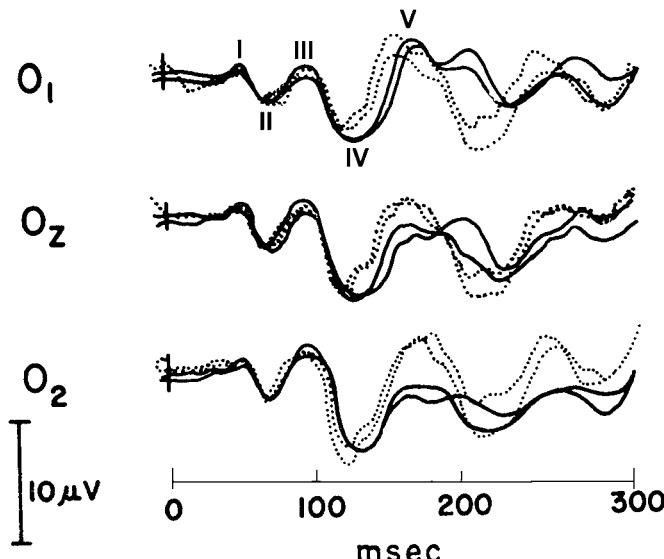
Concomitant recording of electroretinogram (ERG) with VEP can aid in differentiating if a VEP abnormality is reflected by a retinal disease or dysfunction of the central visual pathway. The ERG to flash stimulation is generated by cells in the outer and inner nuclear layer of the retina (F-ERG) and the ERG to pattern stimulation is generated by the ganglion cells in the inner nuclear layer (P-ERG).<sup>73</sup> Both F- and P-ERGs consist of an initial negative a-wave, and subsequent positive b-wave. Both a- and b-waves are larger in amplitude and shorter in latency in F-ERG than in P-ERG. Both F- and P-ERGs require the use of corneal lens electrodes and pupil dilation for quantitative analysis. The ERG (either flash or pattern) recorded by surface electrodes placed near the periorbital skin referenced to a distant site (such as the mastoid) can be used only as a screening examination. The ERG recorded with corneal electrodes is required to verify suspected abnormality noted by ERG recorded with surface periorbital electrodes.

P-ERG is best recorded with a large field (>9 degrees) and with check sizes of 30' to 60'.<sup>74</sup> P-ERG consists of initial negative with latency of about 30 ms (N30) followed by relatively large positive (P50) and broad negative waves (N95).

## STEADY STATE VEP

Increasing stimulus rates above 6 Hz, either by pattern reversal or strobe flash stimulation, produces rhythmic trains of waves of the same frequency as the stimulus rates. This is similar to the photic driving response seen in routine EEG recording. Because the responses are extracted by averaging, a more detailed analysis is possible by this steady-state VEP, as compared to the photic driving response seen in routine EEG testing. The response amplitudes become progressively smaller as the stimulus rate increases.

The steady-state VEP is assessed by phase lag and amplitude at various stimulus rates. The time difference between each peak of the VEP and stimulus is expressed by a phase lag, which changes depending on the stimulus rates. The amplitude decreases progressively with the faster stimulus rates, and eventually disappears. Generally, the highest frequency to flash stimuli at which the response can be recognized (critical frequency) is about 60 to 70 Hz. Although steady-state VEPs have been investigated in patients with MS and optic neuritis,<sup>75,76</sup> or occipital infarction or tumor with visual field defects,<sup>77-79</sup> it has not been popularized as a routine visual function test. This is because of interindividual variability of amplitude and difficulty in establishing strict criteria for determining the presence or absence of the steady-state VEP at different frequencies. However, if there is greater than 10 Hz difference in critical frequency between two eyes in the same subject, it is reasonable to conclude that the eye with the lower critical frequency is abnormal.



**Figure 2-14.** Examples of VEP to strobe flash. In contrast to the simple waveform of pattern reversal checkerboard stimulation, FVEP consists of multiple waves, I through V, within 200 ms after the stimulus. Two tracings from each eye are superimposed. Waves I to III are relatively consistent but IV, V and subsequent waves show inter-trial variability. Because there is considerable inter- as well as intraindividual variability in FVEP, it is difficult to determine normality and abnormality in clinical application. (From Kooi KA, Yamada T, Marshall RE. Binocular and monocular visual evoked responses in differential diagnosis of psychogenic and disease-related visual disorders. *Int J Neurol* 1975;9(3):272–286, with permission.)

## VEP BY OTHER STIMULATION

### FLASH AND LED GOGGLE VEPS

The VEP can be elicited by stroboscopic flash light using the same stimulus device used in routine EEG studies. The flash VEP (FVEP) can be elicited with eyes closed or during sleep, or even in a comatose state. The response generally consists of a series of negative-positive peaks, named waves I, II, III, IV, V, etc within 200 ms after the stimulus (Fig. 2-14). Although FVEP usually has a robust response, there is considerable interindividual variability in the waveform and latency, and it is difficult to establish reliable normative data. As a consequence, FVEP has never developed into a clinically useful diagnostic test. The same interindividual variability applies to LED stimulus, often using LED goggles. LED goggles placed over the eyes can be used for infants or subjects who are too uncooperative to reliably fixate upon pattern stimuli. LED or FVEP can also be used for patients who have severe refractive errors. Assessment relies only on the presence or absence of a response, not on latency, waveform, or amplitude measures.

### OTHER STIMULUS DEVICES FOR VEP

There are many other stimulus devices available. There are sine-wave grating stimuli, bar-grating stimuli, color stimuli, moving and stereoscopic random-dot pattern stimuli, and macular light spots stimuli, etc. These are primarily used for various research projects and not for routine clinical use, and therefore these will not be discussed here.

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# Brainstem Auditory Evoked Potentials and Auditory Evoked Potentials

## ANATOMY OF AUDITORY PATHWAY IN BRAINSTEM

The brainstem auditory evoked potential (BAEP) deals with the auditory pathway within the brainstem. Sounds entering the ear canal cause a vibration of the tympanic membrane of the external ear. The sound waves are then amplified by a piston-like function of three ossicles (small bones consisting of the malleus, incus, and stapes) in the middle ear. This is received by the cochlea, where the mechanical vibration from the stapes bone is converted into pressure waves, stimulating the hair cells of the organ of Corti. The organ of Corti serves as an auditory frequency analyzer. The activation of hair cells sends the impulses to the cochlear nerve. The cochlear nerve is a part of the VIII cranial nerve (auditory or vestibulocochlear nerve), which also includes the vestibular nerve (Fig. 3-1). The vestibular nerve receives impulses from the semicircular ducts that respond to movements of the head. The vestibular system relates to coordination in the eyes, neck, and body for maintenance of posture and movement of the head.

The impulses from the cochlear nerve enter the brainstem at the upper medulla, close to the junction of the medulla and the pons. It then reaches the anterior and posterior cochlear nucleus (Fig. 3-2). After synaptic connection at the cochlear nuclei, the axons from these nuclei enter the superior olive nuclei. Some fibers stay on the same side, while others cross to the opposite side. After the olive nuclei, fibers ascend the lateral lemniscus at the pons via the nuclei of the lateral lemniscus. The ascending fibers make a synaptic connection at the inferior colliculus of the midbrain and the medial geniculate body. After the sensory relay station at the medial geniculate body, the final path reaches the primary auditory sensory cortex situated at the anterior-superior temporal gyrus (gyrus of Heschl, Brodmann's area 41 and 42). It is important to recognize that the auditory nerves receive bilateral input; therefore, a central lesion affecting only one side of the brain or brainstem does not cause deafness. Deafness in one ear usually indicates a lesion at the cochlear nerve.

## BRAINSTEM AUDITORY EVOKED POTENTIALS

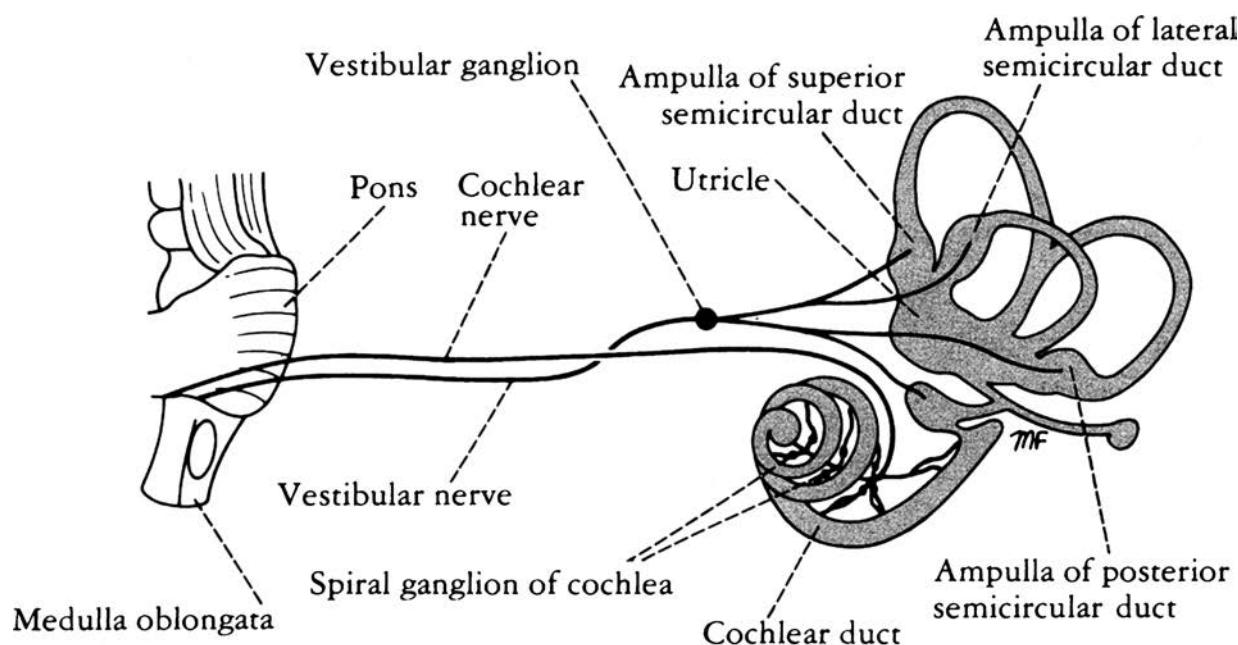
The brainstem auditory evoked potential (BAEP) was the first clinical application to utilize the far-field potential. The far-field potential (FFP) was introduced by Jewett et al.<sup>1</sup> who discovered a series of wavelets (called "Jewett bumps" named after his pioneering work) following auditory stimulations. Unlike the conventional evoked potentials or action potentials (APs) that are best recorded from electrodes near the generator source, the BAEP is recorded from electrodes a distance from the generator source, that is, the auditory pathway within the brainstem. The potentials can be recorded from a wide area of scalp electrodes as a result of a volume conduction spread through brain tissue, CSF, skull, and scalp (Fig. 3-3). One can perceive the FFP as if the distant scalp electrode is examining the events occurring in the brainstem via a telescope. FFPs are generally of positive polarity and are considered to represent positive dipole fields that appear at a distance from the generator source. The negative field more commonly occurs near the generator source. Each wave of the BAEP (except for wave I) is generated when the auditory impulse passes through a specific portion of the auditory pathway within the brainstem. The generation mechanisms of FFPs are better delineated later by somatosensory evoked potentials and will be discussed in more detail in Chapter 4 of this section. Wave I is not an FFP but a near-field potential, picked up by the ear reference electrode on the side of stimulation, generated as a negative potential by the cochlear nerve before the entrance into the brainstem.

## TECHNICAL PARAMETERS

### STIMULATION

#### *Stimulus Types*

The stimulus used for BAEP is a click delivered through an earphone. The click is a broad-band sound, delivering a wide range



**Figure 3-1.** Schematic model of the anatomy of the cochlear duct and the semicircular duct in relationship to cochlear nerve and vestibular nerve. The VIII cranial nerve (auditory and vestibulocochlear nerves) serves two separate functions. One is the auditory function via cochlear duct and cochlear nerve. The other is the balance/coordination function via semicircular duct and vestibular nerve. The ampullas of lateral, superior and posterior semicircular ducts serve as a vestibular function. The cochlear duct and spiral ganglion of cochlea serve as an auditory function. (From Snell RS. *Clinical Neurophysiology for Medical Students*, 5th ed. Baltimore, MD: Lippincott Williams & Wilkins, 2001, with permission.)

of audio frequencies. These clicks are generated by 100- $\mu$ s rectangular pulses. The sound pressure waves elicited by a monophasic square wave pulse consist of a single large wave followed by multiple wavelets lasting up to 2 ms (Fig. 3-4). These sound pressure waves activate the tympanic membrane. Click stimuli that have a sudden onset are suitable for eliciting BAEP but not suitable for audiologic studies because they consist of multiple frequencies. For testing a specific frequency sound, tones with a fixed frequency must be used. Since tone frequency, especially a low-frequency tone, requires a long duration, it may not be suitable for BAEP but may be used for medium or long latency auditory evoked potentials (AEP) or event related potentials (ERP) (see page 48 in this chapter, "Auditory P300 ERP"). Tone pips or bursts have symmetrical rising and falling phases, and the rise, fall, and plateau time can be electronically controlled. These are "narrow-band" stimuli that are best suited for the audiologic applications of BAEP or AEP.

### Stimulus Polarity

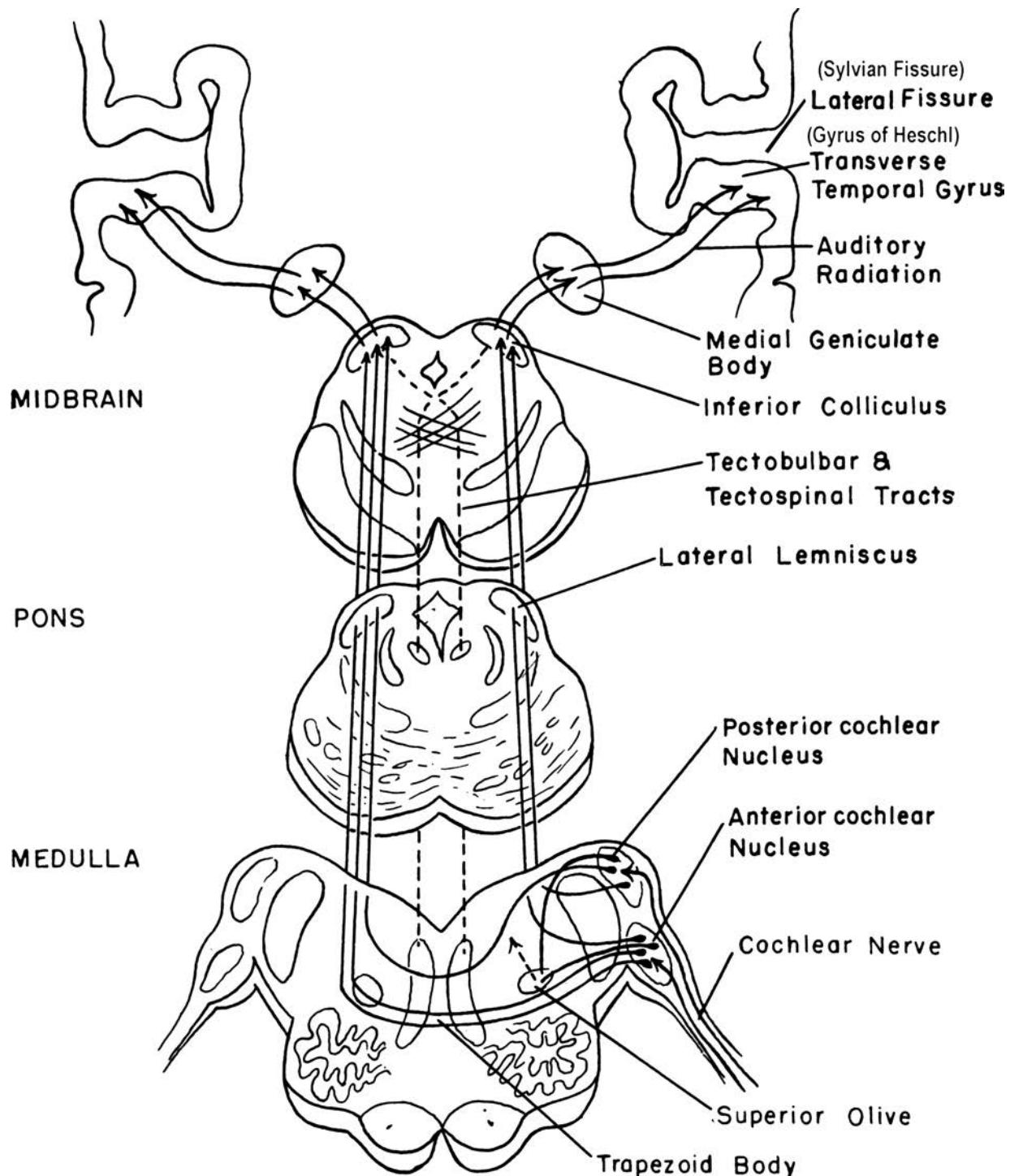
The polarity of the click is determined by the initial movement of the earphone diaphragm: negative pressure that causes the diaphragm to move away from the tympanic membrane is termed "rarefaction click." Positive pressure moves the diaphragm toward the tympanic membrane and is called "condensation click" (see Fig. 3-4). The polarity of the stimulus artifact or the cochlear-microphonic response (see page 37 in this chapter, "Electrococleogram") to the condensation and rarefaction click is opposite (see Figs. 3-4, 3-7, and 3-8). Generally, the rarefaction click is used more often than the condensation click. But there is no clear rationale as to which click polarity to use. Whether to use the rarefaction or condensation click is a matter of laboratory preference. But one should use the same

polarity that was used while collecting normative data. On some occasions, alternating clicks may be used to reduce the stimulus artifact or cochlear-microphonic responses (see Fig. 3-7). However, it should be noted that the waveform and latency may be altered depending on which click polarity is used.

### Stimulus Intensity

Stimulus intensity is expressed in decibels (dB), which is a logarithmic unit of sound intensity. There are four terms used in quantifying sound intensity: sound pressure level (SPL), peak-equivalent sound pressure level (peSPL), hearing level (HL), and sensation level (SL). The first two are pure physical measures of intensity. SPL is based on measuring an arbitrary zero reference point set at 0.0002 dyne<sup>2</sup>/cm<sup>2</sup> (20 micropascals). Because the actual pressure of a brief sound is difficult to measure, peak-equivalent sound pressure level (peSPL) is used by measuring the peak-to-peak amplitude of a sine wave that is equal to the amplitude of a given tone or click to be measured. The maximum intensity sound that is considered to be safe is about 110 to 120 dB peSPL. The highest intensity available in most commercial auditory stimulators is 105 to 110 dB peSPL. A group of normal subjects has a threshold of approximately 30 dB peSPL.

Hearing level (HL) is the average threshold intensity of hearing in normal young adults, and zero dBHL is then defined as the average threshold for this group of normal adults. If a subject is stimulated with 80-dB peSPL by an auditory stimulator and hearing threshold (HL) of the normal group is measured at 30 dB peSPL, the stimulation intensity is then 50 dBHL (80 dB peSPL - 30 dB peSPL = 50). An alternative scale for stimulus intensity is expressed by the sensation level (SL), which is the hearing threshold of an individual ear (rather than of a

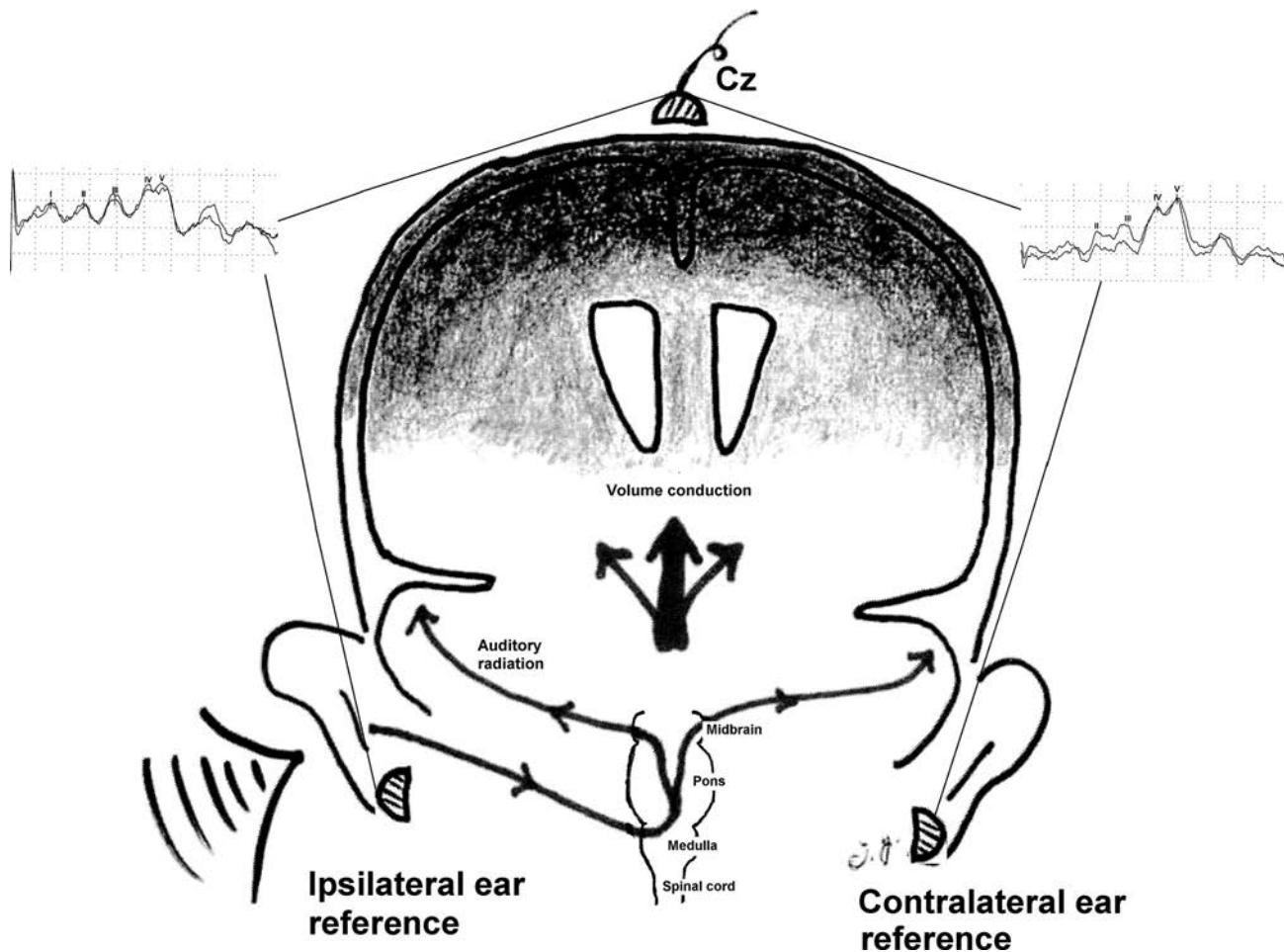


**Figure 3-2.** Schematic model of auditory pathways. The impulse carried through the cochlear nerve enters the brainstem at the upper medulla. The impulse then ascends through the cochlear nuclei, superior olivary nuclei, lateral lemniscus, inferior colliculus, medial geniculate body, and finally reaches the primary hearing cortex at the superior gyrus of the temporal lobe (gyrus of Heschl). Note some of the fibers cross to the contralateral side and some remain ipsilateral. (From Gatz. *Manter's Essentials of Clinical Neuroanatomy and Neurophysiology*. F.A. Davis Company, 1970.)

normal group). HL and SL are the same in a normal hearing young subject. For example, when the hearing threshold in the left ear is 30 dB peSPL and the right ear is 40 dB peSPL, 90 dB peSPL to both ears delivers 60 dBSL to the left and 50 dBSL to the right ear. In order to deliver a stimulus with the same inten-

sity to both ears, the right ear must be increased by 10 dB peSPL (to deliver 60 dBSL to both ears) or the left ear must be decreased by 10 dB peSPL (to deliver 50 dBSL to both ears).

A hearing threshold for each ear must be determined before the BAEP examination. This can be accomplished by delivering



**Figure 3-3.** Schematic model of far-field potential (FFP) recording. As the impulse passes through the auditory nerve, medulla, pons, and midbrain, multiple waves are generated. These waves spread diffusely via volume conductive media (not via the anatomical pathway of auditory input to the temporal lobe) and can be detected over a wide area of the scalp. The vertex (Cz) electrode is one of the electrodes that can record the FFP. Waves II through V are recorded with either the ipsilateral or the contralateral ear (to the side of stimulation) reference electrode, but wave I is recorded only with the ipsilateral ear reference because wave I is not FFP but a near-field potential with negative polarity at the ipsilateral ear reference.

a relatively low-intensity stimulus and then increasing the intensity by 5-dB steps until the subject starts to hear the sound. Once the sound is perceived, increase the intensity by 10 to 15 dB and then decrease the intensity by 5 dB until the subject can no longer hear the stimulus. If two attempts yield different values, choose an intensity in between the two measures.

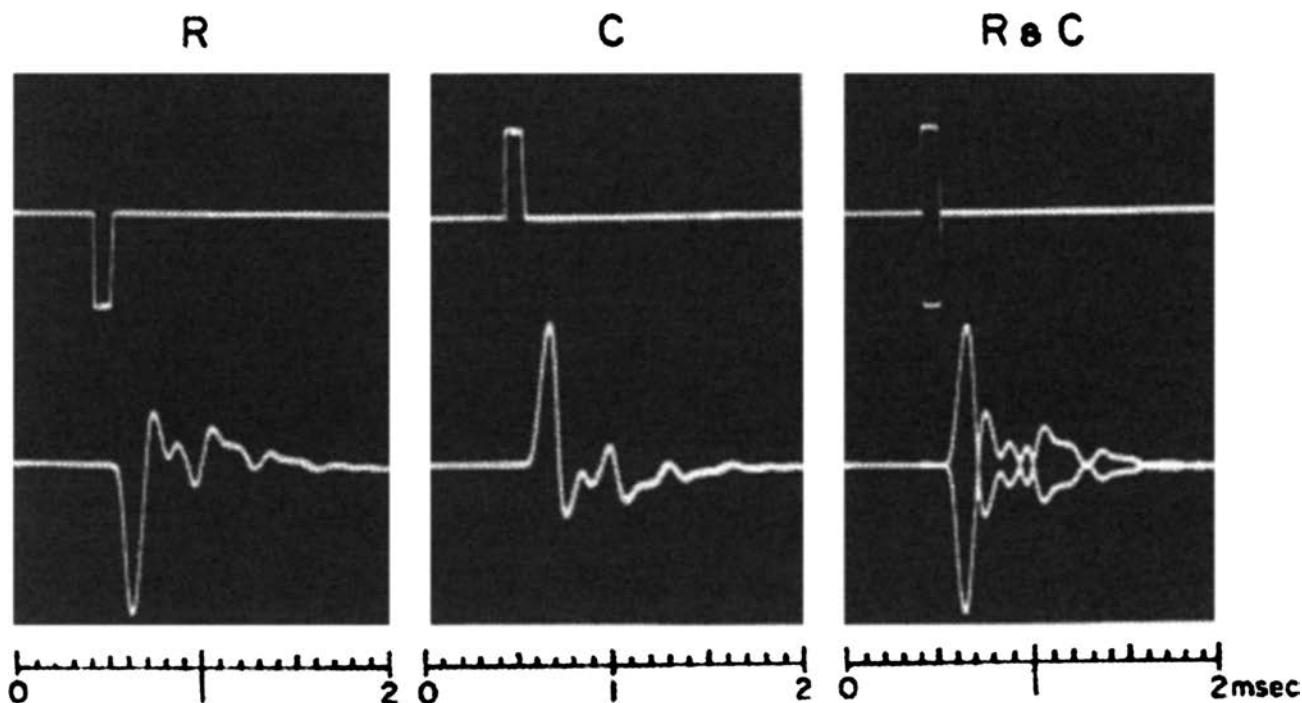
#### Stimulus Rate and Summation

Since BAEP deals with waves that occur within 10 ms after the stimulus, a relatively fast stimulus rate can be used without affecting the response. Generally, 8 to 15 Hz is used for diagnostic BAEP recording. Theoretically, the stimulus rate can be increased up to 100 Hz, but this will attenuate the response. Because BAEP amplitude is small (generally <1  $\mu$ V), the number of summations required will be greater than for VEP or SSEP; generally, 1,500 to 2,000 trials or more are used to yield a reliable and measurable response. In order to minimize 60 Hz interference from power lines, stimulus rates that are multiples of 60, such as 10, 12, or 15 Hz, should be avoided. Commonly

used frequencies are 11.1 Hz, 11.3 Hz, etc. Indeed, some manufacturers automatically offset the stimulus rate such that a multiple of 60 does not occur. For recording long latency AEPs that extend to 500 ms, a stimulus rate of 1 Hz or less must be used.

#### Mode of Stimulation and Masking Noise

BAEPs examine each ear separately (monaural stimulation). The stimulus, applied through an earphone to one ear, can be transmitted to the opposite ear via bone conduction. Although the stimulus is attenuated as it travels across the head through the skull, the intensity conducted through the bone may be sufficient to elicit a response in the opposite ear. This is particularly true when the hearing level is significantly different between the two ears. The ear with poorer hearing will require a higher stimulus level which may be strong enough to adequately stimulate the opposite (non-stimulated) ear. This cross stimulation via bone conduction can be minimized by the delivery of constant masking noise through an earphone on the ear opposite to the



**Figure 3-4.** The sound pressure waves triggered by 100- $\mu$ s rectangular pulse. Note the opposite polarities of rarefaction (*R*) and condensation (*C*) clicks.

stimulated ear. The intensity of masking noise is about 60 dB peSPL or 40 dBSL below the intensity of the stimulated ear.

#### FILTER SETTING

BAEP consists of multiple high-frequency components reaching a frequency of close to 1,000 Hz. Thus, the high-frequency filter should be no less than 2,000 Hz; generally, 2,500 to 3,000 Hz is used. The low-frequency filter setting is 10 to 30 Hz, but may be increased to 100 Hz. Once the band pass filter is set in obtaining normal control data, the setting should not be changed because it can have an effect on the latency of the peaks.

#### ANALYSIS TIME

The analysis time is usually 10 to 15 ms. An analysis time of 15 ms is used for neonatal recordings. Longer analysis time may be used for extremely delayed responses.

#### RECORDING ELECTRODES

BAEP is recorded with a vertex (Cz) to ear derivation. Unlike other evoked potentials, the exact electrode location at Cz is not critical because the response can be recorded over a wide area of the scalp due to volume conducted FFP (see Fig. 3-3). Generally, two channels are used.

Channel 1: Cz-Ai (ipsilateral to the ear being stimulated)

Channel 2: Cz-Ac (contralateral to the ear being stimulated)

Additional channels with an Ac-Ai derivation may be used to delineate wave I. Different waveform characteristics between the

Cz-Ai and Cz-Ac recordings are useful to identify each wave. In order to express positive waves in an upward deflection, Cz is connected to input 1 (grid 1) and Ac or Ai is connected to input 2 (grid 2). This assumes that the EP instrument is designed to show a more positive polarity in input 1 as an upward deflection. (Unlike the EEG amplifier, most EP instruments designate an upward deflection as positive if input 1 is more positive relative to input 2).

#### NORMAL BAEP

Within 10 ms after the stimulus, seven waves are ordinarily identified. These waves are commonly labeled with Roman numerals, I to VII (Fig. 3-5). Since waves VI and VII are inconsistent and not commonly used for diagnostic evaluation, we deal here only with waves I to V. Identifying each wave correctly is important for the evaluation of the BAEP. In addition to the latency and waveform characteristics of each wave, differences between Cz-Ac and Cz-Ai recordings aid in identifying each wave.

Early studies suggested that each wave originated from discrete anatomical structures along the auditory pathway<sup>2,3</sup>:

Wave I: acoustic nerve

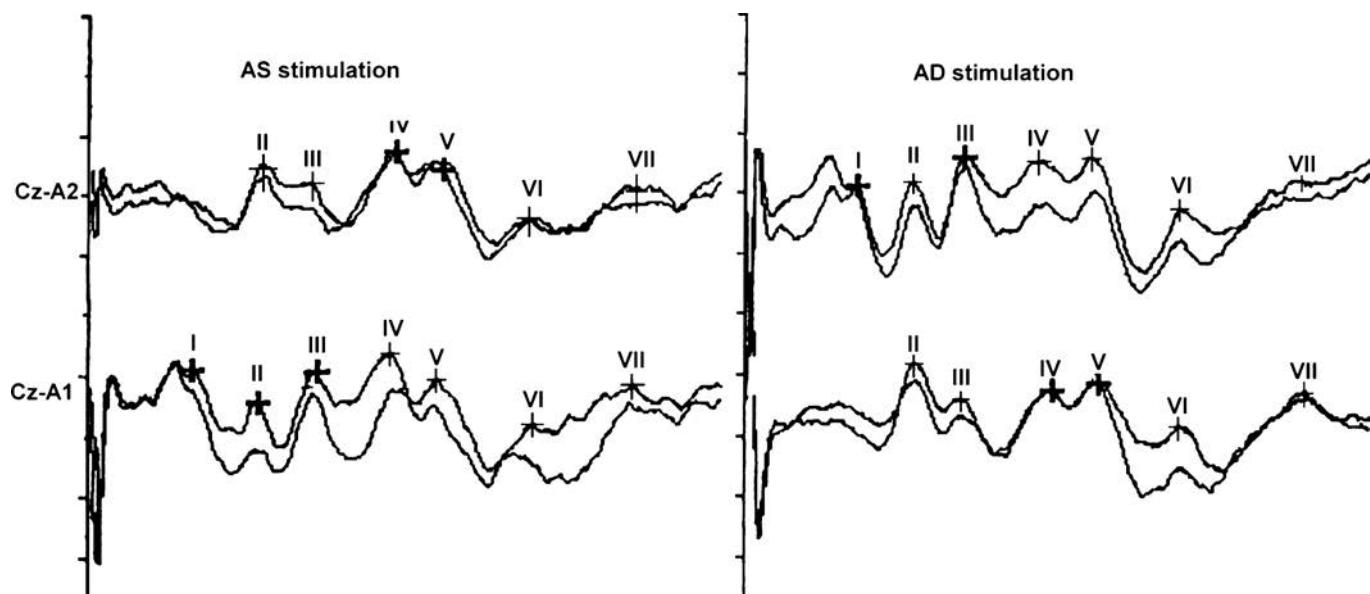
Wave II: cochlear nucleus and trapezoid body

Wave III: superior olivary nucleus

Wave IV: lateral lemniscus

Wave V: inferior colliculus

However, later studies have raised doubts about the discrete origin of each wave. For clinical purposes, it is generally regarded that waves I-III represent the lower brainstem (from upper medulla to midpons) and III-V represent the upper brainstem (midpons to lower midbrain) (see Fig. 3-12).



**Figure 3-5.** An example of typical normal BAEP by AS (left ear) and AD (right ear) stimulations. Note wave I appears only on the ipsilateral ear reference recording. Wave II tends to be larger on the contralateral ear reference, while wave III tends to be larger on the ipsilateral ear reference recording. Waves VI and VII are not consistently identifiable waves. Note a small additional peak preceding wave I, which is a summation potential.

### WAVE I

This wave is recorded only from the Cz-Ai derivation. When wave I is present on the Cz-Ac derivation, crosshearing to the non-stimulated ear via bone conduction may be present, and increased intensity of masking noise is needed. Unlike other waves that are of positive polarity at Cz, wave I is a negative potential arising from the stimulated ear (Ai). The negativity at input 2 (Ai) thus results in the same upward deflection as the later positive peaks that are of positive polarity at input 1. Wave I is a near-field potential that appears near the stimulated ear and represents the volley of the auditory nerve (cochlear nerve) action potential (AP). Wave I latency matches with the negative peak of the AP of electrocochleography and originates near the cochlea (see Fig. 3-8). A higher amplitude of wave I can be recorded from an electrode placed in the external ear canal. Wave I may have multiple peaks. In this case, the last peak before the downward swing should be chosen as wave I (see Fig. 3-5). The earlier peak may be a summation potential or cochlear microphonic potential (see page 37 in this chapter, “Electrocochleogram” and also Fig. 3-8).

Wave I latency is usually 1.5 to 2 ms in children older than 2 years and in adults when an intensity of 70 dBSL is used. The latency is rarely shorter than 1.4 ms or longer than 2.5 ms at 70 dBSL in normal subjects. Wave I latency will increase and the amplitude will decrease with a lower stimulus intensity. At 20 dBSL, the latency may be close to 3 to 4 ms. Wave I is often difficult to elicit in patients with a hearing deficit; however, various technical modifications (see page 42 in this chapter, “Technical modification to improve waveform identification”) may be used to bring it out.

### WAVE II

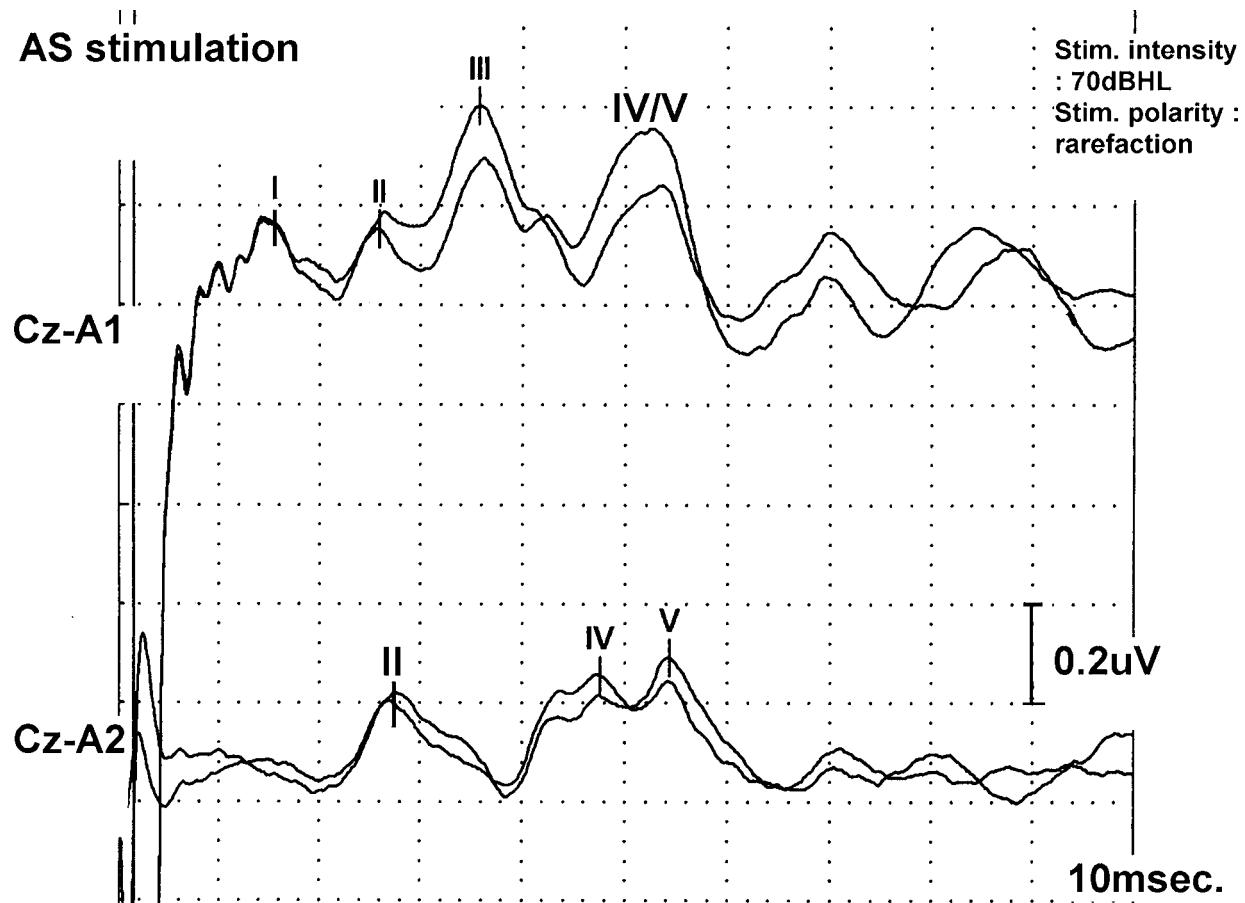
Wave II appears less consistently compared to the other peaks, and may have a higher amplitude and a slightly longer latency with Cz-Ac than with Cz-Ai recording (see Fig. 3-5). The evidence suggests that wave II is at least partially generated by the intracranial portion of the acoustic nerve entering at the rostral medulla.<sup>4-7</sup>

### WAVE III

Wave III appears approximately halfway between Waves I and V. This wave has generally higher amplitude and may be of slightly shorter latency at the Cz-Ai than Cz-Ac recording.<sup>8</sup> Wave III is generated at the level of the superior olfactory nucleus or the lower half of the pons.<sup>2,5</sup> An intact wave I to III in patients with lesions at the upper half of the pons<sup>5,9</sup> is consistent with this view. Wave III may occasionally have two peaks. In this case, either a midpoint or the first peak may be used for wave III identification. Changing the click polarity may bring out a single peak.

### WAVE IV/V COMPLEX

Wave IV/V is generally the largest of all the five waves and appears with various configurations. When separated, either wave IV or V has a higher amplitude peak, or when fused, wave IV may appear on the rising phase of wave V or wave V may appear as a small notch over the descending phase of wave IV. Waves IV and V are better delineated with the contralateral than the ipsilateral ear recording (Fig. 3-6). When fused, the latency of wave V or the IV/V complex may be slightly shorter with an ipsilateral ear recording. The latency of wave V usually falls between 5 and 6 ms at 70-dBSL intensity and should never be shorter than 5 ms. The large downward swing below the baseline following wave V may help to identify wave V. The latency prolongs progressively with decreasing stimulus intensity and may reach 7 to 8 ms at 20 dBSL (see Figs. 3-10 and 3-11). When wave V identification is not certain, decreasing the stimulus intensity may help to identify it. With progressive decrease of stimulus intensity, the other peaks will drop out and the last remaining wave will be wave V (though with an increased latency). With decreased stimulus intensity or in patients with a severe hearing deficit, wave V may be the only wave identifiable. The available evidence suggests that the IV/V complex is generated in the high pons or the low midbrain at the level of the lemniscus<sup>10</sup> or the inferior colliculus.<sup>11,12</sup>



**Figure 3-6.** An example of a fused IV/V complex seen in ipsilateral reference recording. The waves IV and V are better delineated using the contralateral reference recording.

## ELECTROCOCHLEOGRAM (ECochG)

ECochG is best recorded from an electrode placed in the external auditory canal referenced to the nose or the contralateral ear. ECochG consists of cochlear microphonic, summation potential and AP.

### COCHLEAR MICROPHONIC (CM) POTENTIALS

CM potentials arise from phasic reaction of cochlear hair cells and the potentials appear as a series of rhythmic wavelets merging with or overriding wave I of the BAEP, especially when high-intensity stimulus is used (Figs. 3-7 and 3-8). Because condensation and rarefaction clicks cause opposite polarities in the cochlear microphonic, adding the responses of rarefaction and condensation clicks or using alternating click polarity effectively abolishes the cochlear microphonic response (see Figs. 3-7C and 3-8). Conversely, the cochlear microphonic is enhanced by subtracting the rarefaction response from the condensation response (see Fig. 3-8B).

### SUMMATING POTENTIAL

The summing potential (SP) is another small negative deflection that appears just before wave I of the BAEP. Unlike a cochlear microphonic, the polarity remains the same irrespective

of the click polarities. The SP represents the receptor potential of the cochlear hair cells (Fig. 3-8C).

### ACTION POTENTIAL (AP)

The AP is a compound nerve action potential generated by the primary auditory nerve fibers (see Fig. 3-8A,C). This corresponds to wave I of the BAEP. Its latency increases and amplitude decreases with decreasing stimulus intensity. If the BAEP does not show a discernible wave I, recording the AP using an electrode placed on the wall of the external ear canal near the tympanic membrane can elicit an AP or wave I. Similar to SP, addition of rarefaction and condensation responses enhances the AP.

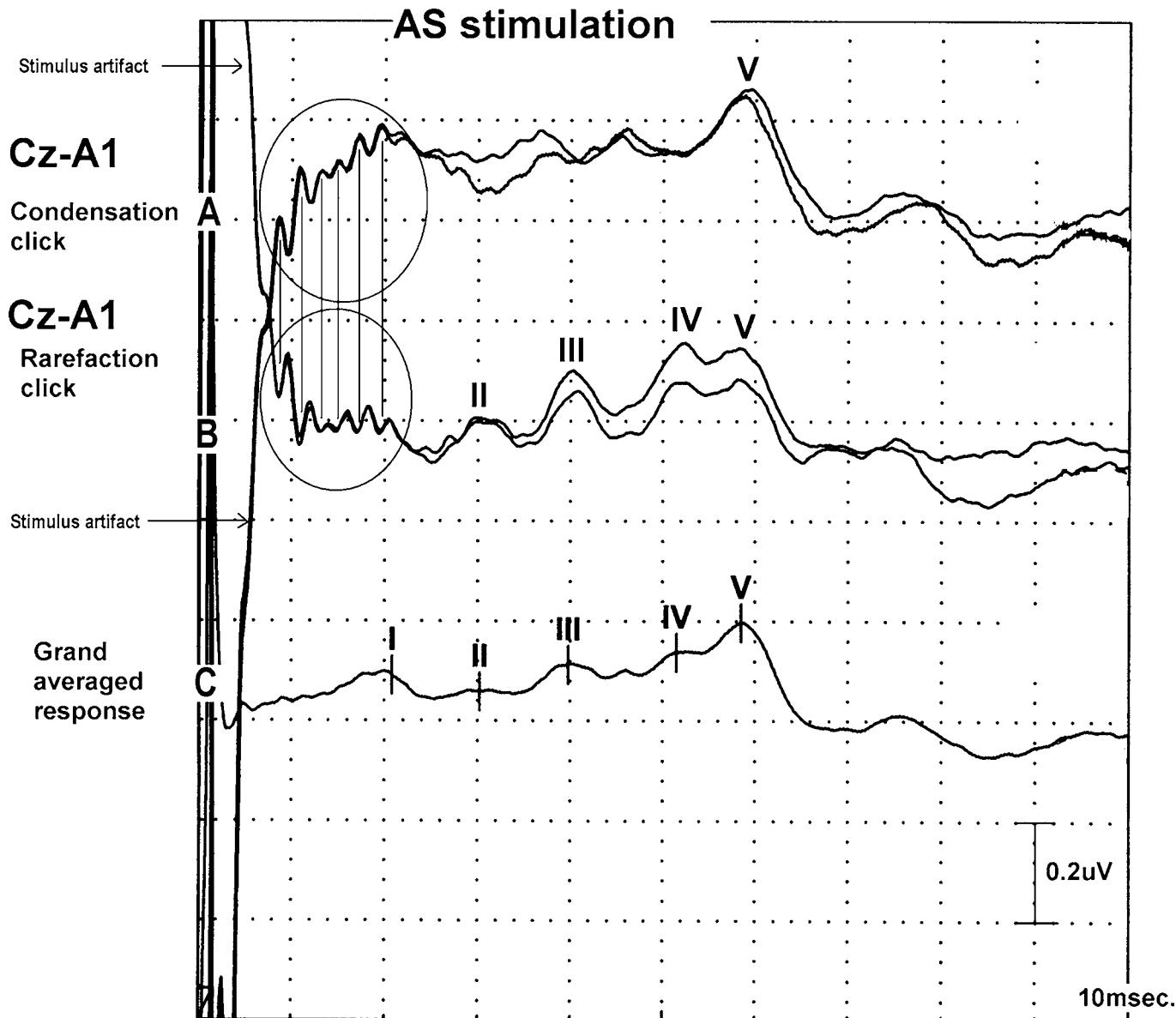
## FACTORS THAT AFFECT BAEP

### PHYSIOLOGICAL FACTORS

#### Age

BAEPs change dramatically in neonates and infants before the age of two. In premature and neonatal infants, waveforms have a simple appearance, often consisting of wave I and V only (Fig. 3-9). The adult configuration is reached by 3 to 6 months.

At a conceptional age (CA) of 33 weeks (preterm), mean latencies of waves I, III, and V are 2.6, 5.7, 8.2 ms, respectively,



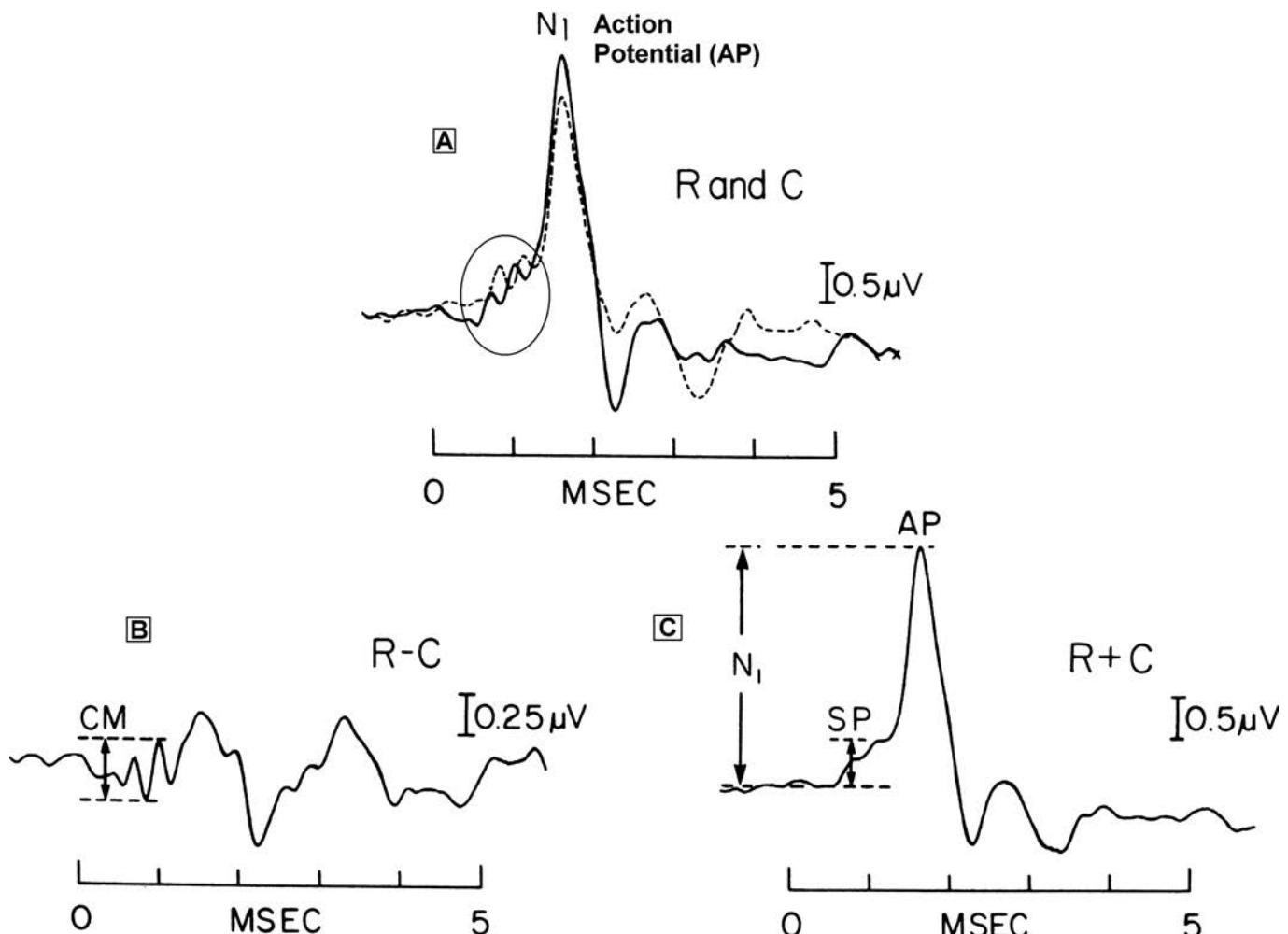
**Figure 3-7.** An example of cochlear microphonic (CM) potentials recorded by condensation and rarefaction click. Note the out-of-phase relationship of CM potentials and stimulus artifacts between rarefaction and condensation click recording. Adding both responses reduced CM potentials as well as stimulus artifacts that aid in better delineating wave I.

with a I-V interpeak latency (IPL) of 5.6 ms.<sup>13</sup> Wave V latency then progressively decreases approximately 0.2 ms/wk.<sup>14,15</sup> At 40 weeks CA (full term), mean latencies of Waves I, III, and V are 2.3, 5.1, and 7.5 ms with a I-V IPL of 5.2 ms.<sup>13</sup> The latency continues to shorten after 40 weeks' CA and reaches adult levels at 2 to 3 years.<sup>15,16</sup> These rapid changes require the establishment of normal data with short intervals; every 2 weeks for premature babies, then at 3, 6, and 12 weeks, 6 months, and 1 year of age.

Conflicting reports have been published for the BAEP changes of advancing age. Some studies reported an increase of the I-VIPL,<sup>17,18</sup> while another study did not find this aging effect.<sup>19</sup> Because these differences are so small, no age-specific standards for the elderly have commonly been applied in clinical practice.

#### Gender

It has generally been agreed that females have shorter absolute latency as well as IPL and higher amplitude than males<sup>8,19–21</sup>. This gender difference starts after the age of 8 years.<sup>22</sup> The differences have been attributed to head size, skull thickness and/or brain size. The male/female latency ratio is calculated as  $1.03 \pm 0.008$ .<sup>23</sup> For routine clinical application, the gender is not considered because the difference is small and within the limit of measurement variations. In detailed research work, however, gender difference must be taken into account to establish detailed normality and abnormality.



**Figure 3-8.** An example of electrocochleogram (ECochG) in relationship to rarefaction and condensation clicks. **B** and **C** are the same data as **A** manipulated off line. **A** shows responses of rarefaction (*R*: solid line) and condensation (*C*: broken line) superimposed. Note the initial small rippling wavelets (CM potentials) with an out-of-phase relationship (shown by circle), but subsequent large negative potentials (AP) are in phase between the *R* (Rarefaction) and *C* (Condensation) responses. **B** shows an enhanced CM potential and attenuated AP by subtracting the *C* from *R* response. **C** shows attenuation of CM potential and enhanced AP (corresponds with wave I of BAEP) and preceding summation potential (SP) by adding *C* and *R* responses. (From Coats. *Arch Otolaryngol* 1981;107:199, with permission.)

### Body Temperature

A decreased body temperature prolongs the absolute and interpeak latencies; 1°C temperature drop may increase the wave V latency exponentially by 0.17 ms<sup>24</sup> or by 7%.<sup>25</sup> BAEP becomes “flat” at temperatures below 27°C.<sup>26,27</sup>

### Drug Effect

Therapeutic doses of CNS depressant drugs or anesthetic doses of pentobarbital, ketamine, halothane, and chloralose do not affect the BAEP.<sup>28</sup> BAEP is unaffected by barbiturate doses high enough to show electrocerebral silence (ESC) on an EEG.<sup>29</sup> Also phenothiazine, benzodiazepine, or short-acting barbiturates have no effect on the BAEP.<sup>30</sup> Alcohol intoxication<sup>31,32</sup> and toxic levels of diphenylhydantoin<sup>33</sup> may cause a slight prolongation of the I-V IPL. In general, drug effects in evaluating BAEP can be ignored. This is one of the advantages for the use of BAEP in intraoperative monitoring.

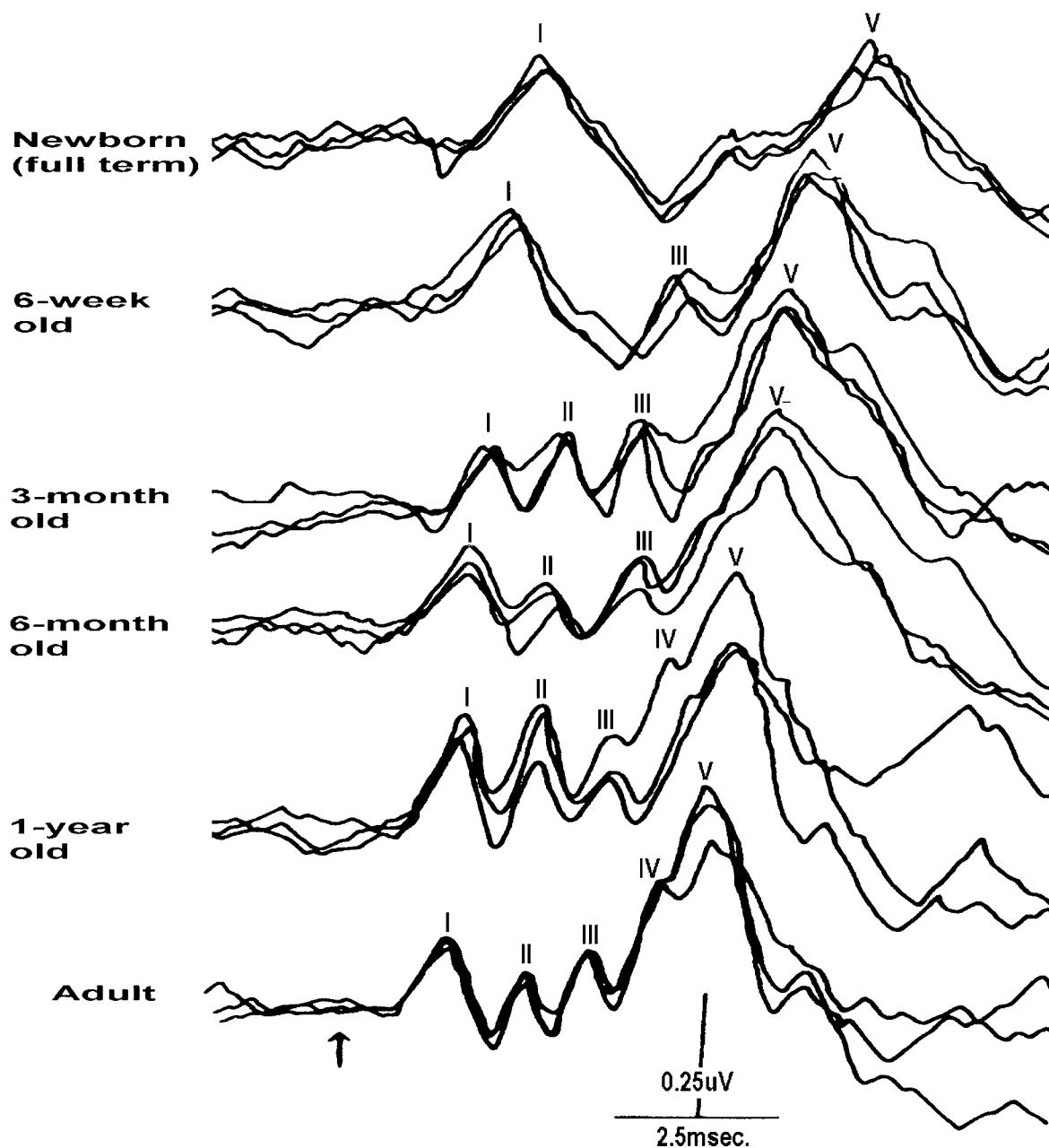
### Factors Relating to Consciousness

BAEP is not dependent on level of consciousness, cognitive function,<sup>34,35</sup> or sleep.<sup>36</sup> This is beneficial for diagnostic applications of BAEP because these factors can be ignored, especially for testing in infants and children.

### NONPHYSIOLOGICAL FEATURES

#### Click Polarity

Rarefaction click is more commonly used than condensation click. The former tends to show slightly shorter wave I and V latencies, more distinct wave IV and V, and larger wave I.<sup>37-39</sup> The above features are by no means consistent and show considerable individual variations. Although adding rarefaction and condensation responses or using alternating clicks is technically useful to minimize stimulus artifacts and cochlear microphonic responses, this should not be used as a routine practice. It should

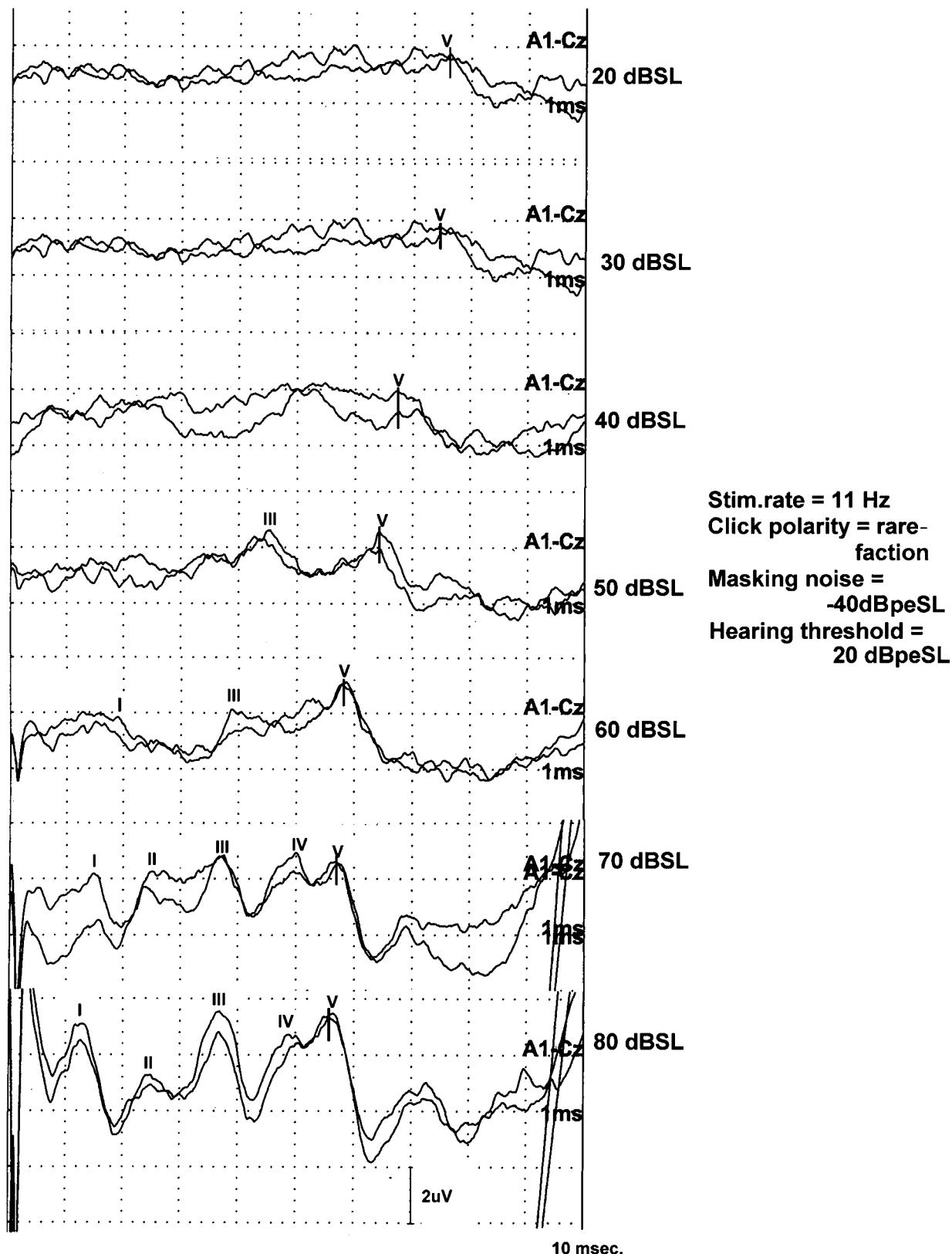


**Figure 3-9.** BAEP age differences from newborn to adult. Only waves I and V are well identified with prolonged absolute latencies and I-V IPL in newborn. Note the progressive shortening in both absolute latency and I-V IPL with aging. At 1 year old, absolute latencies and IPLs become close to adult values. (From Salamy, McKean. *Electroencephalogr Clin Neurophysiol* 1976, with permission.)

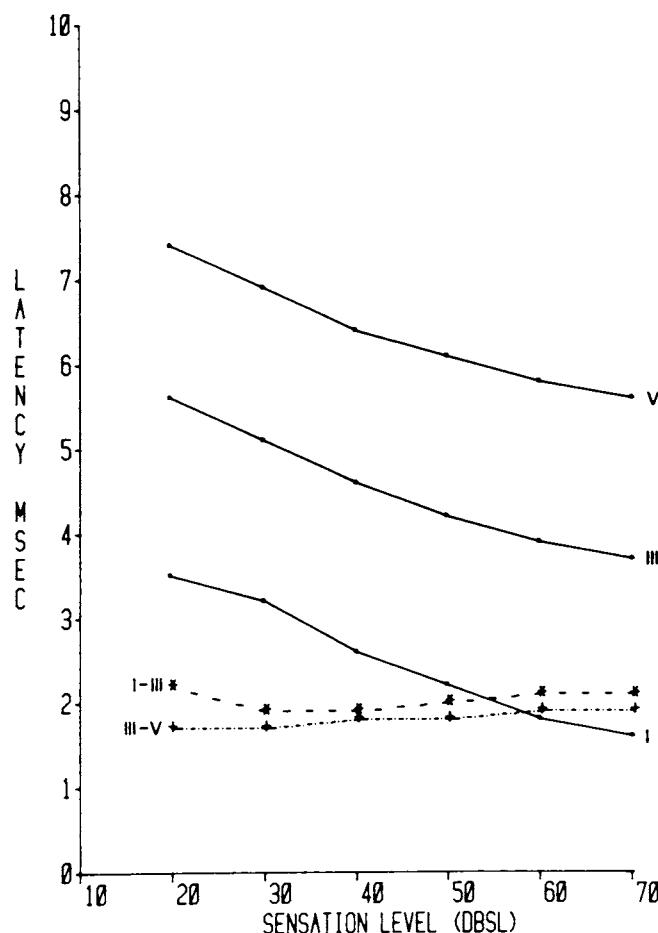
be noted that waveforms and latencies of rarefaction and condensation responses may not always be the same, and adding the two may significantly alter the response. In some cases, wave V may be absent with one polarity but not with the other.<sup>39</sup> It is debatable if this should be considered abnormal or normal. We have seen a patient with basilar migraine in which an abnormal BAEP was observed only with the rarefaction and not with the condensation click during the migraine attack.<sup>40</sup> Further systematic study is needed to establish clinical correlates of discrepant responses between rarefaction and condensation stimulation.

#### Stimulus Intensity

Decreasing stimulation intensity results in a decrease in amplitude and an increase in latency (Fig. 3-10). The latency increase is roughly linear with 0.3 ms per 10-dB decrease of stimulus intensity. Because the latencies of all BAEP waves shift nearly in parallel, the IPLs show little change<sup>41,42</sup> (Fig. 3-11). The consistency of the IPL irrespective of stimulus intensity is convenient for neurologic applications of BAEP. In detail, however, there is a slight difference between high- and low-intensity stimulation with



**Figure 3-10.** The waveform and latency change with decreasing stimulus intensity in a normal subject. Note progressive increase of latencies and decrease of amplitude on all waves with decreasing stimulus intensity. Wave V is the last identifiable potential with weak stimulus intensity.



**Figure 3-11.** Latency change with changing stimulus intensity. Note the near linear and parallel prolongation of wave I, III and V with decreasing stimulus intensity. Because of this near parallel change, I-III and III-V IPLs change little with changing stimulus intensity. (From Chiappa. Evoked potential. In: *Clinical Medicine*. Philadelphia, PA: Lippincott-Raven, 1997.)

slightly shorter IPL with low-intensity stimulus (e.g., 30 dBSL compared with 70 dBSL; see Fig. 3-11) primarily due to slightly greater prolongation of wave I compared to other peaks.<sup>43</sup>

When there is a difficulty in identifying wave V, a progressive decrease of stimulus intensity aids to clarify wave V by noting that wave V latency prolongs almost linearly and is the last wave to remain.

When waves IV and V are merged, decreasing the intensity may bring out a better separation of waves IV and V.

In patients who have significant hearing deficits, for example, with a hearing threshold of 60-dB peSPL, the maximum deliverable stimulus intensity is only 50 dBHL (with maximum deliverable stimulus intensity of 110-dB peSPL). This will result in a prolongation in all waves or an absent wave I and subsequent waves. Wave V may be the only wave that can be identified. In this case, the assessment must rely on a latency-intensity curve to determine if the hearing deficit is due to a conductive (such as mechanical blocking of the ear canal by cerumen) or a sensorineural (nerve damage) problem (see Fig. 3-13).

### Click Frequency

The broad click sounds contain a wide range of frequencies ranging from 500 to 4,000 Hz. These tend to stimulate larger areas of the cochlea more than the pure tone stimuli that consist of more restricted frequencies.<sup>44</sup> Waveforms by the usual click intensities (60–70 dBSL) are primarily generated from the cochlea that responds to 2,000 to 4,000 Hz frequencies.<sup>45</sup> A more restricted frequency of click or tone pips consisting of 500 to 2,000 Hz may be used for audiologic studies to achieve more frequency specific BAEP or AEP examinations. Since changes in frequency alter the latency and amplitude of the BAEP, it is important to use the fixed frequency that was used for collecting normal data.

### Stimulus Rates

Commonly used stimulus rates are 8 to 11 Hz. The rates can be increased up to 70 to 100 Hz. However, faster stimulus rates (>30 Hz) may lose some components of BAEP waveforms.<sup>44,46,47</sup> Also, increased stimulus rates slightly prolong the IPL.<sup>44,46,48</sup> Increasing the stimulus rate to more than 30 Hz may worsen the abnormality or increase the incidence of abnormality not revealed by the usual rate (about 10 Hz).<sup>49–51</sup>

### TECHNICAL MODIFICATION TO IMPROVE WAVEFORM IDENTIFICATION

1. Stimulus artifact is too large and obscures wave I.
  - a. Decrease the impedance of recording and ground electrodes.
  - b. Adjust the location of input cables and stimulus cables; separate these two cables.
  - c. Decrease stimulus intensity.
  - d. Use alternating clicks or add rarefaction and condensation responses.
  - e. Replace the earphone.
2. Wave I is not identified
  - a. Increase stimulus intensity.
  - b. Change click polarity.
  - c. Decrease stimulus rate.
  - d. Use alternating click or add rarefaction and condensation responses; this reduces the stimulus artifact and also eliminates the cochlear microphonic response but may alter the waveform.
  - e. Use ear canal electrode.
  - f. Use Ai-Ac derivation, which enhances wave I relative to other waves.
3. Wave V is difficult to distinguish from wave IV.
  - a. Decrease stimulus intensity; this may separate a fused IV/V.
  - b. Use contralateral ear reference recording, which usually shows better separation of IV and V.
4. Wave V is difficult to differentiate from wave IV or VI.
  - a. Decrease stimulus intensity. When stimulus intensity is progressively decreased, wave V is the last wave to remain.

Identifying wave V recognized by low stimulus intensity allows estimation of wave V latency obtained by the higher stimulus intensity.

## EVALUATION OF THE BAEP

Most laboratories use latency prolongation of 2.5 or 3 standard deviations (SD) above the mean as the abnormal criteria. This applies to both absolute latency and IPL. The amplitude criteria are less reliable because the values do not follow a Gaussian (normal) distribution.

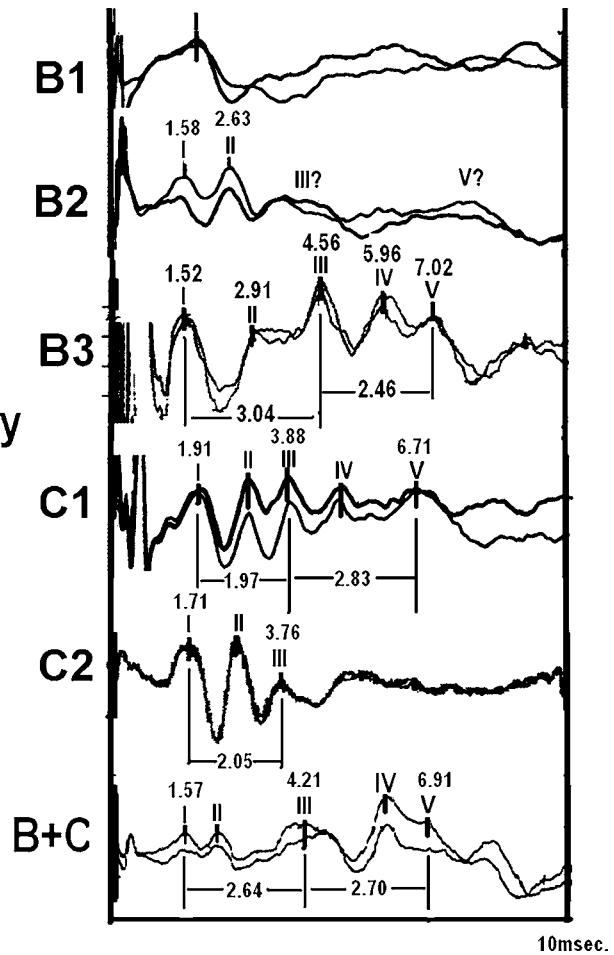
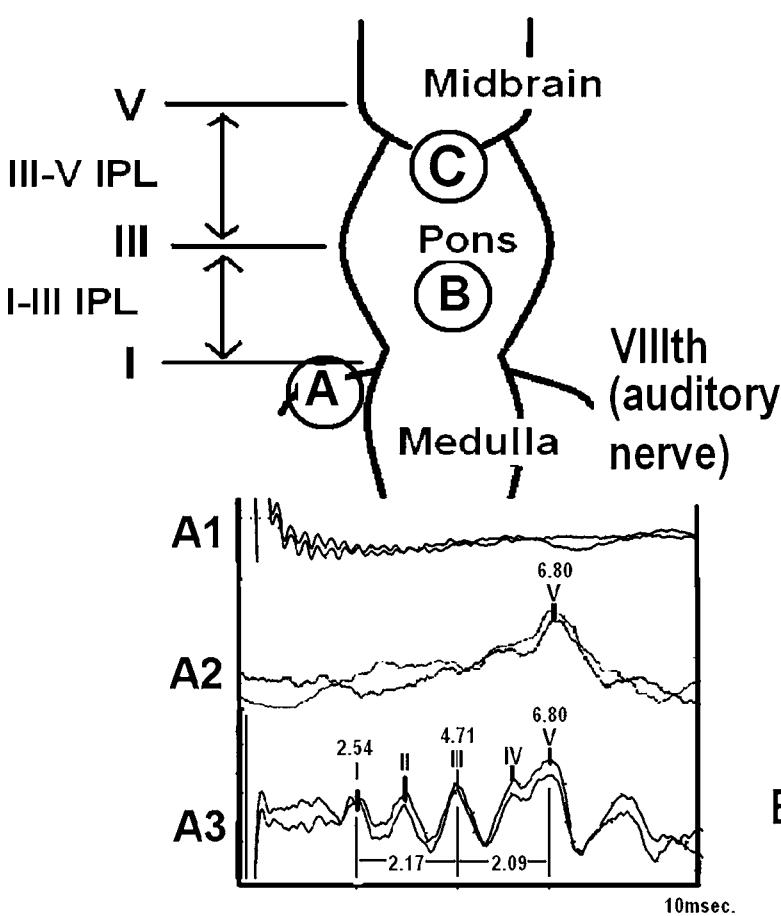
Exact generator sources of each BAEP waveform are not known, but serial activation of each component along the auditory pathway allows fairly accurate localization for lesions within the brainstem. After the auditory nerve enters the brainstem at the upper medulla, large portions of the auditory pathway cross to the opposite side and ascend contralateral to the side of the ear activated. From the anatomical and theoretical points of view, the BAEP waveform, especially the late waves, should represent the contralateral brainstem. However, the majority of clinicopathological studies found that the site of the lesion was ipsilateral to the ear producing the abnormal BAEP.<sup>52,53</sup> For example, an abnormal BAEP to left ear stimulation corresponds to a lesion in the left brainstem irrespective of the components affected. The

following BAEP parameters are to be examined. Because waves I, III, and V are the most consistently measurable components, the abnormal criteria are primarily based on these 3 waves.

### ABSENCE OF ONE OR MORE WAVES

#### *Absence of All Waves*

When no response is elicited, the first consideration is a technical problem. Is stimulus intensity adequate in relationship to the individuals' hearing threshold? Are recording electrodes placed correctly and connected to the amplifier? Is the stimulus rate appropriate? Is the number of responses averaged sufficient in relationship to the noise? Is the signal adequately triggered and amplified? Is the vertical (amplitude) scale adequate to view the wave form? The presence of stimulus artifacts or cochlear microphonic assures that the stimulus adequately triggers the averaging process (Fig. 3-12A1). After all possible technical problems are excluded, the absence of wave I through V indicates severe conductive or sensorineural hearing loss or a lesion at the acoustic nerve. In this case, detailed audiometric testing is indicated.



**Figure 3-12.** Examples of various BAEP abnormalities in relationship to localized lesions at A, B, and C. A lesion at A results in A1, A2, or A3 response. A1 response shows only CM response without wave I through V. A2 response shows absence of all waves but V with prolonged latency. A3 shows all waves with prolonged absolute latencies but normal inter-peak latencies (IPLs). A lesion at B results in normal wave I (or I and II). B1 shows an absence of peaks after wave I. B2 shows normal wave I and II but with delayed and diminished subsequent peaks. B3 shows well-formed, but delayed peaks beyond wave I with delayed I-III IPL. A lesion at C results in normal waves I to III but delayed wave V and prolonged wave III-V and I-V IPLs. C2 shows normal waves I through III and an absent wave V. With diffuse lesion or dual lesions at B and C, waves I-III, III-V and I-V IPLs are prolonged (B + C).

### Absence of Wave I

The absence of wave I with prolongation of wave V is usually associated with a hearing deficit (Fig. 3-12A2). When wave I is not identified, it is necessary to increase the stimulus intensity until wave I is discernible. In some patients, the maximum allowable stimulus intensity (105–110 dB peSPL) may not be high enough to elicit wave I because of a high hearing threshold. The absence of wave I excludes the measurement of I-III or I-V IPL, but waves III and V may be present. The absence of wave I but with a normal wave V with peak latency of less than 6 ms, however, should be considered to be a normal response.

### Absence of Wave II and Subsequent Waves

This finding suggests a retrocochlear lesion involving the proximal intracranial portion of the auditory nerve (Fig. 3-12B1).<sup>7,11,54</sup> Brain dead patients may show this pattern. The absence of wave II alone with other normal waves should not be considered abnormal.

### Absence of Wave III and Subsequent Waves

A lesion at the level of the superior olfactory complex may obliterate wave III and subsequent waves (Fig. 3-12B2).<sup>9</sup> Similar to wave II, the absence of wave III alone should not be considered abnormal, if waves I and V are normal.

### Absence of Wave IV/V Complex or Decreased V/I Amplitude Ratio

Complete absence of wave V indicates a lesion at the midbrain or the rostral pons (Fig. 3-12C2). Decreased amplitude of wave V with normal latency presents difficulty in determining the abnormality. Generally, wave V is larger than wave I, but this is affected by stimulus intensity and hearing loss. The ratio tends to decrease with higher stimulus intensity. Although the V/I amplitude ratio less than 0.25 or 0.5 may be arbitrarily considered abnormal, it is best to be rather conservative in using this parameter to determine wave V abnormality, especially when wave V latency is normal. Decreased amplitude with prolonged wave V latency is clearly an abnormal finding (Fig. 3-12C1).

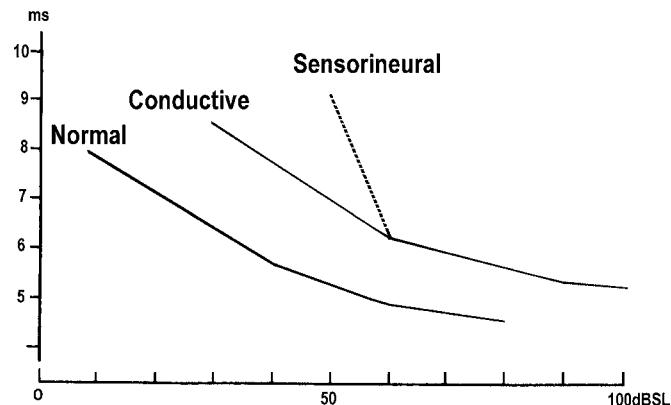
## LATENCY ABNORMALITIES

### Absolute Latency Values

The evaluation of absolute latency values must be correlated with stimulus intensity. This has been used mainly in the audiological examination for hearing evaluation, but has some limitation because (i) determining hearing threshold is difficult at times and (ii) the test involves only high-frequency sound, not the frequency of the speech range.

In patients with hearing deficit, wave I is often absent or delayed, and wave V may be the only wave identified (Fig. 3-12A2). Wave V latency increases nearly linearly with decreasing stimulus intensity (see Figs. 3-10 and 3-11). A delayed wave I with normal I-III, III-V, or I-V IPL is consistent with conductive or sensory-neural hearing loss (Fig. 3-12A3).

The relationship between latency and intensity is demonstrated by a latency-intensity curve that plots wave V latency values against stimulus intensity (HL) in 10-dB increments



**Figure 3-13.** Schematic model of “Latency-Intensity Curves”. In *normals*, wave V latency prolongation occurs near linearly with progressive reduction of stimulus intensity. In *conductive* hearing loss, latency prolongation is near parallel with normal curve but with prolonged absolute latency. In *sensorineural* hearing loss, the latency prolongation is non-linear with a sudden nonparallel prolongation or abrupt loss of wave V at a certain decreased stimulus intensity (in this case at 60 dBDSL).

(Fig. 3-13). Patients with conductive hearing loss show prolonged wave V latency and near-parallel prolongation with a normal latency-intensity curve. In patients with sensorineural hearing loss, a stepwise reduction of stimulus intensity results in a nonparallel prolongation or abrupt disappearance of wave V at a certain level of stimulus intensity.

### Interpeak Latency

Interpeak latency (IPL) evaluation requires identifying at least two or three waves (Waves I, III, or V). The IPLs are measured between I-III, III-V, and I-V by subtracting the latency of one from the other. The upper limit of normal IPL for I-III is generally 2.5 ms, III-V is 2.4 ms, I-V is 4.7 ms at 70 dBDSL in most laboratories (Table 3-1). Since IPL is only minimally affected by stimulus intensity or hearing deficit, this is a convenient and simple measure to evaluate the auditory pathway within the brainstem. Increased I-III IPL suggests conduction slowing in the brainstem auditory system between the acoustic nerve and the lower pons. (Fig. 3-12B3) An abnormally prolonged III-V IPL suggests a conduction slowing between the lower pons and the midbrain (Fig. 3-12C1). An increased I-V IPL is usually associated with prolonged I-III, or III-V IPL, or both. Prolonged I-III, III-V, and I-V IPLs indicate a diffuse process or multiple brainstem lesions (Fig. 3-12B,C). An absent wave I with a normal III-V IPL indicates normal conduction between the upper pons and the midbrain but does not allow determining the conduction between the auditory nerve and the lower pons.

There are some exceptions to the rule that increased I-V IPL indicates a central lesion. When the effective stimulus intensity is low relative to severe hearing loss, the IPL may be increased due to greater prolongation of wave V than of wave I. Conversely, in patients with high-frequency hearing loss, I-V IPL may be shortened as a result of a greater increase of wave I than wave V latencies.<sup>55</sup>

<b>TABLE 3.1</b>		<b>BAEP Normative Data</b>							
Absolute	I	II	III	IV	V	IPL	I-III	III-V	IV
Mean	1.51	2.66	3.63	4.72	5.61	Mean	2.12	1.98	4.10
SD	0.13	0.12	0.15	0.17	0.21	SD	0.14	0.13	0.16
Upper limit	1.90	3.02	4.08	5.23	6.24	Upper Limit	2.54	2.37	4.58
<i>L-R difference</i>	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>		<i>I-III</i>	<i>III-V</i>	
Upper limit	0.2	0.3	0.2	0.3	0.2		0.4	0.3	0.4

The above values are in milliseconds.

### Prolonged Absolute Latencies of All Waves with Normal IPL

This abnormality is seen commonly in patients with a moderate degree of hearing loss, either conductive or sensorineural (Fig. 3-12A3, see also Fig. 3-13). Increased stimulus intensity may normalize the latencies. The same conditions occur when the stimulus intensity is too low relative to the subject's hearing threshold.

### Prolonged Wave V with Absence of Preceding Waves

Since IPL cannot be measured in this condition, it is not possible to distinguish a central vs. peripheral lesion (Fig. 3-12A2). Audiologic or latency-intensity curve evaluations should be performed. Further increase of stimulus intensity or change of click polarity may bring out other waves.

### Interauricular Differences

IPLs should also be measured comparing the two ears. The upper limit of normal is generally close to 0.4 ms. If the difference is greater than 0.5 ms, it is definitely abnormal (Table 3-1). The interauricular absolute latency difference is less reliable because this may be due to the difference in hearing threshold or effective stimulus intensity between two ears.

## CLINICAL APPLICATION OF BAEP

BAEP has been utilized for the diagnosis of multiple sclerosis (MS), cerebellopontine angle tumor, coma, hearing deficit, and other diverse conditions. The test is a sensitive tool for the assessment of the integrity of the brainstem auditory pathway and nearby structures. "Immunity" to the level of consciousness or various drugs also increases the diagnostic utility of BAEP. Abnormal BAEPs are, however, etiologically nonspecific and final diagnosis must be based on other clinical information.

### MULTIPLE SCLEROSIS (MS)

Like other evoked potential studies, BAEP can reveal clinically silent brainstem lesions that other tests may fail to diagnose. A number of BAEP studies in MS have been published.<sup>53,56-60</sup> The abnormal incidences vary considerably from one study to the other presumably due to the difference in definition of the MS diagnosis, abnormal criteria, and technical variations. Overall abnormal rates are 60% to 70% for definite, 40% for probable, and 30% for possible group of MS patients. These figures are lower than those of VEP and SSEP, likely because BAEP deals

with an anatomically shorter pathway than VEP or SSEP. About one fifth to one half of MS patients with no clinical evidence of brainstem signs or symptoms have an abnormal BAEP.

Various types of BAEP abnormalities have been found in MS ranging from prolonged IPLs to absence of part or all of the waves except wave I (see Fig. 3-12). The most common abnormality is the absence or the severe depression of wave V, followed by prolongation of I-III IPL.<sup>58</sup> BAEP abnormalities may increase or decrease during the course of the illness, and this may or may not correlate with clinical changes.<sup>56,60</sup> Serial BAEPs, therefore, may not be useful for monitoring changes in clinical condition or disease progress.

A faster rate of stimulation (70 Hz) has been reported to yield a higher incidence of abnormalities,<sup>56,61</sup> but this has not been confirmed by other studies.<sup>58,62</sup> Some MS patients may have abnormality to only one polarity of click stimulus, rarefaction, or condensation, more commonly by the former.<sup>39,63,64</sup>

### CEREBELLOPONTINE (CP) ANGLE TUMORS

BAEP is a highly sensitive test for acoustic neuroma or meningioma impinging on the brainstem.<sup>4,65-69</sup> Because acoustic neuroma involves the acoustic nerve, wave I is usually affected with absence or latency delay. The absence of wave I makes it difficult to differentiate from nonspecific hearing loss, either conductive or sensorineural. Successful identification of wave I, using the best available techniques (including external auditory canal electrode), would improve the diagnostic specificity for CP angle tumors since compression of the brainstem commonly causes I-III IPL prolongation. In fact, prolongation of I-III IPL is the most sensitive measure with very small false-negative results. BAEP may be abnormal even when neuroimaging studies are normal. Conversely, if I-III IPL is normal or less than 2 SD beyond the mean, the presence of an acoustic neuroma is unlikely. An increase of I-III or III-V IPL may occur ipsilaterally or contralaterally to the side of the lesion as a result of brainstem distortion.<sup>67,70</sup>

### COMA AND BRAIN DEATH

The use of BAEP for assessment of coma is limited unless the lesions involve the auditory pathway in the brainstem. Also, coma secondary to metabolic or toxic encephalopathy usually shows a normal BAEP.<sup>71</sup> Space-occupying lesions in the cerebral hemisphere or widespread post-traumatic or post anoxic cerebral damage usually do not show abnormal BAEPs unless the lesion extends caudal to the midbrain. There have been a number of studies that deal with the relationship between BAEP and clinical outcome in comatose patients after head injury.<sup>7,72-75</sup>

The prognostic value of BAEP is limited and less accurate than SSEP. This is presumably because the BAEP is limited to brainstem function while SSEP includes functional integrity of both the brainstem and cerebrum. Nonetheless, the complete absence of BAEP bilaterally strongly correlates with poor outcome if the absence is not due to the damage of the peripheral auditory pathway.

Patients who fulfill the criteria of brain death show no BAEP after wave I or occasionally after wave II.<sup>2,76-79</sup> When the EEG is ECS (electrocerebral silence) due to overdose of barbiturate or anesthetic agents, BAEPs are usually normal.<sup>30,80</sup>

### BRAINSTEM TUMOR

BAEP is useful for localizing focal lesions involving auditory pathways within the brainstem. Wave I-III IPL is increased if the lesion is located in the pontomedullary region or lower pons, and III-V is increased for lesion involving the pontomesencephalic junction or midbrain. The incidence of abnormalities in intramedullary tumors, especially gliomas, is close to 100%.<sup>4,9,52,61,80</sup> BAEPs may be abnormal in pinealoma invading the upper brainstem<sup>2</sup> or the cerebellar tumors.<sup>81</sup>

### VASCULAR LESIONS

BAEPs can be normal or abnormal depending on the location of the infarction. Most BAEPs in patients with "locked-in" syndrome are normal<sup>2,52,82</sup> because infarction occurs most commonly in the ventral pons, different from auditory pathways that run more dorsally and laterally. Also, patients with lateral medullary infarcts tend to have normal BAEPs because these lesions are caudal to the level of the auditory nerve entrance at the medulla.<sup>52</sup> Abnormal BAEPs have been reported in patients with Weber's syndrome and Benedict's syndrome.<sup>83</sup> Some patients with transient ischemic attacks involving vertebrobasilar artery territory may have abnormal BAEPs even when they are asymptomatic at the time of examination.<sup>84,85</sup>

### BAEP IN INFANTS AND YOUNG CHILDREN

BAEP provides useful information for the evaluation of hearing ability, CNS deficits, and developmental impairments in infants and young children. BAEP can be best examined during sleep. The stimulus intensity may start with 70-dB peSPL and increase at 5-dB increments until a well-defined response is obtained. The stimulus intensity should not exceed 95-dB peSPL. Because BAEP maturation shows rapid changes within a short time span, it is necessary to evaluate the response based on the normative data according to the conceptional age.<sup>86,87</sup> Only waves I and V might be identified in newborn infants, especially in premature babies (see Fig. 3-9). Infants treated in a neonatal intensive care unit have a significantly higher incidence of abnormal BAEPs than normal full-term babies, and abnormalities often correspond with hearing deficits.<sup>88</sup> Since BAEPs can be recorded in normal newborns at 30-dB peSPL, no response at 40-dB peSPL likely predicts a hearing loss. Abnormal BAEP may also predict motor delay and an abnormal neurological examination.<sup>49,89</sup>

### OTHER DISEASES THAT MAY SHOW ABNORMALITIES IN BAEP

A relatively high incidence of BAEP abnormalities has been reported in leukodystrophy. These include metachromatic leukodystrophy,<sup>90,91</sup> adrenoleukodystrophy,<sup>90-93</sup> Pelizaeus-Merzbacher disease<sup>90,93</sup> and hereditary motor-sensory neuropathy.<sup>94</sup> Less consistent abnormalities of BAEP have been reported in Charcot-Marie-Tooth disease,<sup>95,96</sup> Friedreich's ataxia<sup>49,97-99</sup> amyotrophic lateral sclerosis,<sup>100,101</sup> and olivopontocerebellar degeneration.<sup>102,103</sup>

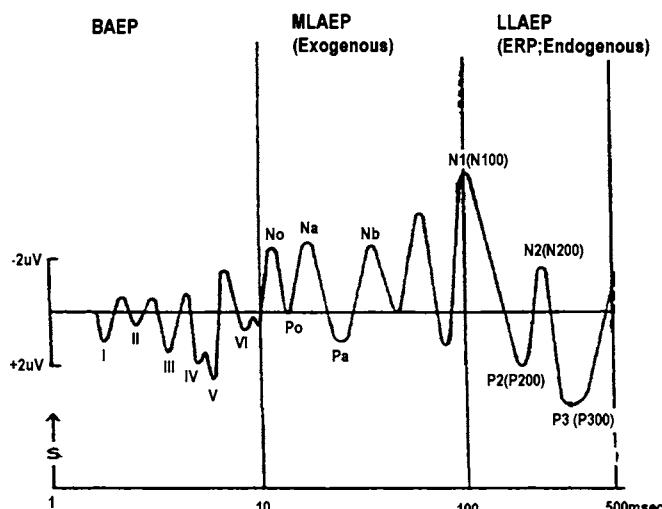
### MIDDLE AND LONG LATENCY AUDITORY EVOKED POTENTIAL

Following the BAEP (which ends 10 ms after the stimulus), the auditory evoked response can be seen as a series of negative-positive waves continuing for as long as 300 to 400 ms. Those waveforms occurring within 50 ms have generally been referred to as "Middle Latency Auditory Evoked Potential," (MLAEP) and the subsequent, longer latency waves are classified as "Long Latency Auditory Evoked Potential" (LLAEP).

Both can be recorded from the vertex with reference at the ear or the mastoid electrode. Unlike BAEP waveforms that are commonly expressed as positive peak upward, MLAEP and LLAEP may be displayed as negative peak upward. Instead of a click stimulus, tone bursts, tone pips, or filtered clicks are usually used to elicit MLAEP and LLAEP. Since neither are commonly used for neurological diagnostic purposes, only a brief description is presented here.

#### MLAEP

Following wave V of the BAEP, MLAEP consists of a series of negative-positive peaks, named "No-Po-Na-Pa," within 50 ms after the stimulus (Fig. 3-14). Because the waveforms of the



**Figure 3-14.** Latency and wave form differences among BAEP, MLAEP, and LLAEP. (Note the positivity is shown by downward deflection). (Modified from Altenmüller EO, et al. Neurocognitive functions and the EEG. In: Niedermeyer E, Da Silva FL, eds. *Electroencephalography: Basic Principles, Clinical Applications and Related Fields*, 5th ed. Philadelphia, PA: Lippincott Wilkins & Williams, 2005:661-682, Chapter 31, with permission.)

MLAEP are slower than BAEP in its frequency, the optimal frequency band width is 10 to 300 Hz. The stimulus rate is about 1 to 2 Hz. Similar to BAEPs, MLAEPs are resistant to a change in the level of consciousness, attention, or mild sedation.<sup>104</sup> The response may be obscured by neck muscle reflex activity that is time locked to the auditory stimulus and occurs about 10 ms poststimulus.<sup>105</sup>

MLAEP amplitude is about 1 to 2  $\mu$ V, which is larger than BAEP but smaller than LLAEP. Usually 500 to 1,000 response summations would be sufficient to delineate the response. A cortical or a subcortical anatomical origin of MLAEP has not been firmly established. Na, with a latency of 15 to 29 ms, has been thought to originate from mesencephalic structures including the inferior colliculus.<sup>12,106</sup> Pa, with a latency of 25 to 30 ms, has been thought to arise subcortically<sup>107,108</sup> as well as from the auditory cortex.<sup>109,110</sup> Because of much greater test-retest variability than with BAEP, clinical application of MLAEP has been limited. Lesions of the thalamus or the midbrain are more likely to affect MLAEP than cortical temporal lesions.<sup>107,111</sup>

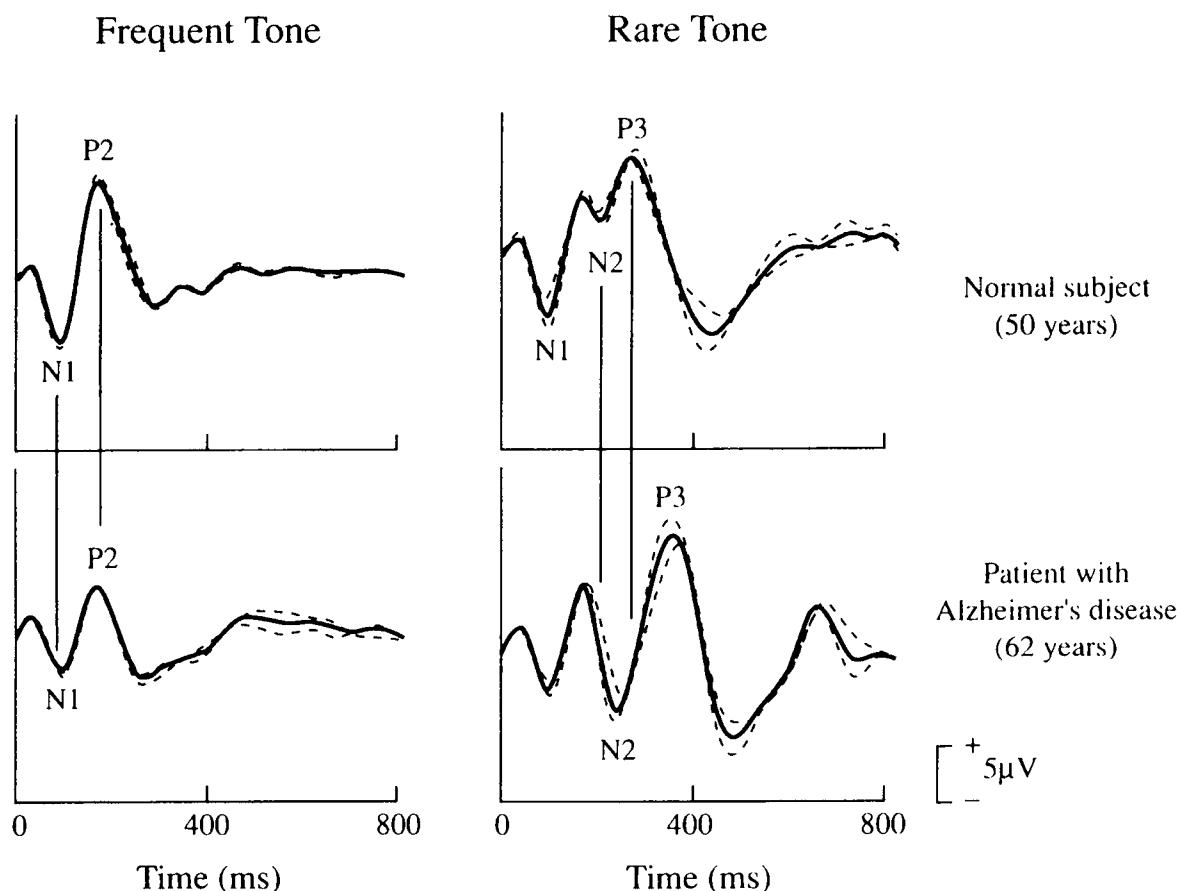
### LLAEP

LLAEP starts with NI, which has a latency of around 100 ms. This is followed by large -positive- negative peaks, referred to

as "P2, N2, and P3" (Fig. 3-15). N1 peak latency occurs at about 100 to 150 ms, P2 at 150 to 200 ms, N2 at 200 to 250 ms, and P3 at around 300 ms. Since LLAEP consists of slower-frequency waveforms than BAEP or MLAEP, the filter settings should be shifted to the lower-frequency bandwidth, less than 1 Hz. for a low filter and 100 to 200 Hz. for a high filter.

The amplitude is larger than BAEP and MLAEP, and less than 100 response summations may be sufficient to delineate the response. Increased stimulus rate decreases the amplitude and increases the latency. While MLAEPs are *exogenous components* that are dependent on purely physiological functions, P2, N2, and P3 are *endogenous components* that are greatly influenced by internal cognitive processes. Increased vigilance, attentiveness to the stimulus, and irregularly spaced slow stimulus rates (to avoid habituation) tend to enhance these endogenous components.

Clinical application of LLAEP for neurological disorders has been limited because of considerable inter- and intraindividual variability of LLAEP. However, sensitivity of LLAEP, particularly the P3 or P300 component, to various cognitive functions has provided useful information for psychological and neurobehavioral evaluations. These are commonly referred to as "auditory event related potentials" (ERP).



**Figure 3-15.** Long latency ERP showing P300 (P3) potential elicited by "odd ball" paradigm in a normal subject and a patient with Alzheimer's disease. P3 was elicited only by rare tone. N1 and P2 are the same in both subjects but P3 latency is clearly delayed in Alzheimer patient. (From Goodin, Aminoff. Electrophysiological differences between subtypes of dementia. *Brain* 1986;109:1103–1113, with permission.)

Since the original description by Sutton in 1965,<sup>112</sup> the most extensively studied ERP has been the auditory P300 or P3. Although P300 can also be elicited by visual and somatosensory stimuli, auditory P300 is most commonly used because the recording technique is relatively simple and P300 responses are robust.

### AUDITORY P300 ERP

#### *Recording Techniques*

Two different types of stimulations, for example, 2,000-Hz. and 1,000-Hz. tones are delivered in a random sequence. One type of stimuli is given infrequently (about 10%–20% of total stimulus) and the other is given frequently. The subject is asked to pay attention to the infrequently occurring stimuli (target stimuli) and ignore the frequent stimuli. The method is named the “oddball paradigm.” In order to maintain attentiveness to the target stimulus, the subject may count the infrequent stimuli or press a key as soon as an infrequent stimulus is perceived. Depending on the interest, a more complex task may be used.

The recording electrodes are Fz, Cz, and Pz referenced to linked ears. The frequency bandwidth is less than 0.5 Hz. for the low-filter and 100 to 200 Hz. for the high-filter setting. The analysis time is usually 500 to 600 ms. The responses for frequent and infrequent stimuli are separately averaged. A total of 20 to 80 summations for infrequent (target) stimuli would be adequate to yield a measurable P300 or P3 potential. An excessive number of summations will deteriorate the response probably due to fatigue, decreased attentiveness, or habituation. During the recording, the subject should be alert but relaxed, minimizing muscle and eye movement artifact.

#### *Normal P300*

Comparison between the responses with frequent and infrequent (target) stimuli shows distinct differences; P300 (P3)

and preceding N200 (N2) appear only in the target response (Fig. 3-15). Both amplitude and latency are affected by age, type of task, and degree of difficulty in differentiating the target stimulus. The amplitude is usually highest at Pz and reaches about 10 to 20  $\mu$ V. The latency ranges from 250 to 500 ms. The amplitude tends to decrease and the latency prolongs with age.<sup>113</sup> The latency of P300 increases with a more difficult task.<sup>114</sup>

A number of theories have been proposed for the generation of the P300; it relates to perception and evaluation of stimulus,<sup>115</sup> orienting reflex to unexpected stimulus,<sup>116</sup> sorting and renewal of memory process in relationship to the target stimulus,<sup>117</sup> or sensory information processing and preparation for the reaction.<sup>114</sup>

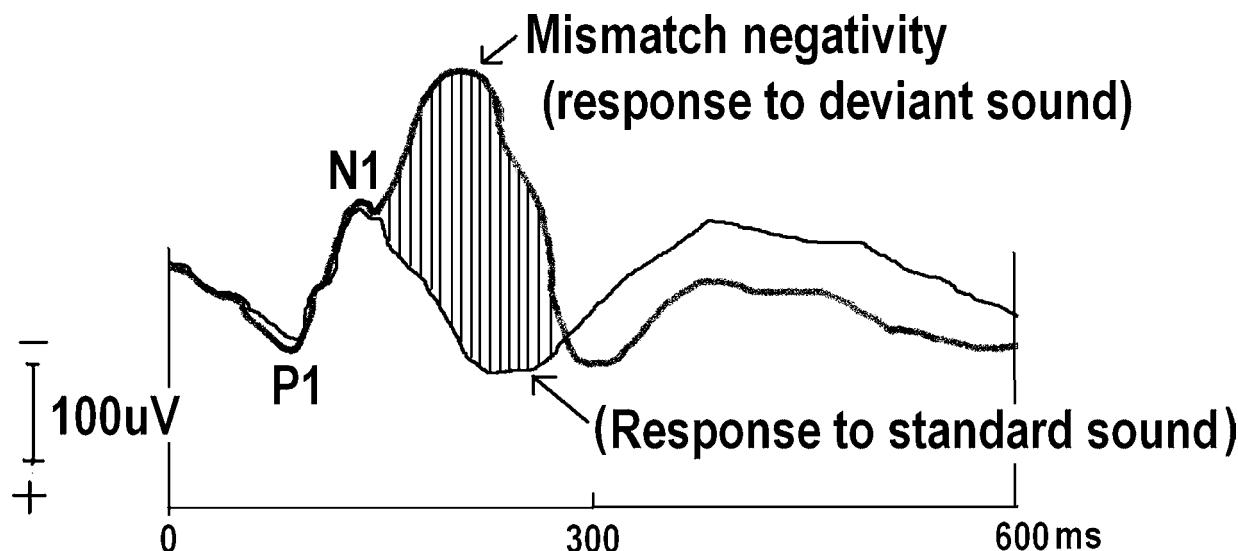
The anatomical origin of P300 is not known. The origins of parietal cortex,<sup>118</sup> thalamus,<sup>119</sup> and hippocampus<sup>120</sup> have been proposed. Perhaps no single anatomical source is responsible for P300 generation. It is more likely a complex connection and intricate interaction of cortical and subcortical structures reflect P300.

#### *Clinical Application*

Because of considerable individual variations, one should be cautious in applying P300 data to an individual case. Group-to-group comparisons have shown that P300 latency is delayed in dementia patients as compared to the age-matched normal controls.<sup>117,121</sup> The amplitude of P300 has been reported to be decreased in schizophrenic patients.<sup>122,123</sup>

#### MISMATCH NEGATIVITY (MMN)

N200 that precedes P300 is referred to as “mismatch negativity” (MMN), which has a different cognitive function from that of P300 (Fig. 3-16). MMN is elicited upon the unexpected perception of a different stimulus character. Because MMN can be elicited without imposing a task, it has been used in infants,<sup>124</sup> children with developmental problems,<sup>125</sup> and comatose patients.<sup>126</sup>



**Figure 3-16.** An example of mismatch negativity elicited by deviant auditory stimulation.

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# Somatosensory Evoked Potentials

## ANATOMY OF THE SENSORY SYSTEM

There are three types of sensory fibers, each carrying different sensations and each having different conduction velocities: (i) pain and temperature senses are carried through the slowest-conducting fibers, (ii) touch and pressure senses are conveyed through medium slow-conducting fibers, and (iii) vibration and position senses travel through the fastest-conducting fibers. Sensory input originates from various types of sensory receptors: These include *free nerve endings*, *Merkel's discs*, *Meissner's corpuscles*, *Pacinian corpuscles*, *Ruffini's corpuscles*, *neuromuscular spindles*, and *neurotendinous spindles*. Each receptor responds to a specific modality of stimulus. The free nerve endings receive pain sensations. Merkel's discs and Meissner's corpuscles react to touch sensations. Pacinian corpuscles receive vibration sense. Ruffini's corpuscles respond when the skin is stretched. Neuromuscular spindles and neurotendinous spindles respond to stretching of muscles and tendons, respectively.

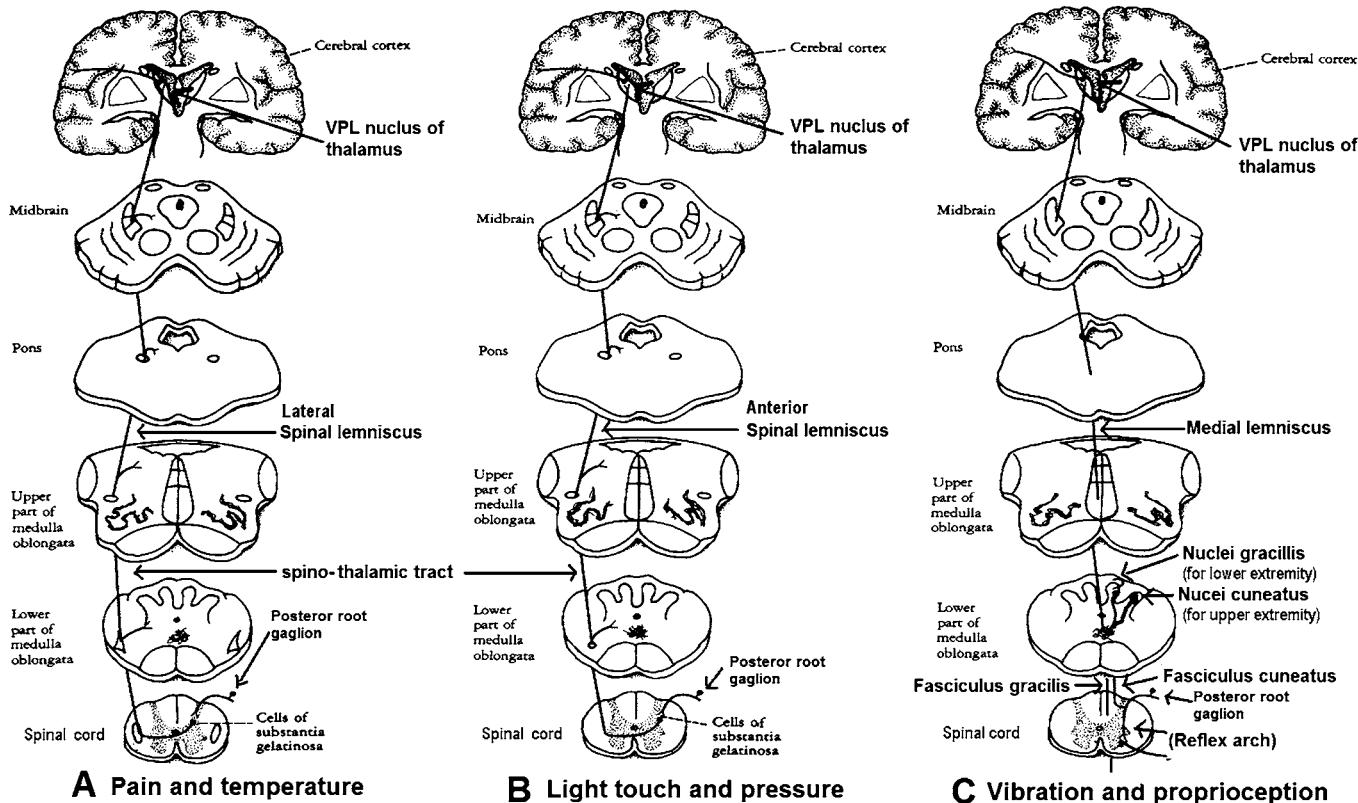
The sensory input received by various receptors then travels through peripheral nerves. There are three types of peripheral nerves: (i) pure sensory nerves, (ii) pure motor nerves, and (iii) mixed nerves that include both sensory and motor fibers. Sensory inputs enter the spinal cord via the posterior spinal roots and then the first-order neurons at the *posterior root ganglion* (Fig. 4-1).

After entering the spinal cord, sensory input travels through different pathways depending on the type of sensation. Pain/temperature or touch/pressure sensations cross to the opposite side of the spinal cord after the synaptic connection at the cells of the *substancia gelatinosa* (second-order neurons) (Fig. 4-1A,B). The pain/temperature and touch/pressure inputs ascend the *lateral spinothalamic tract* and touch and pressure senses ascend the *anterior spinothalamic tract*, respectively. At the brain stem, they ascend as *spinal lemniscus*. The vibration and proprioceptive senses travel on the same side after entering the spinal cord and ascend through the *posterior column* (Fig. 4-1C). The posterior column consists of two *fasciculi*, *fasciculus gracilis* and *fasciculus cuneatus*, which carry sensory inputs from the lower and upper extremities, respectively. The fasciculus gracilis runs medially to the fasciculus cuneatus in the spinal cord. The fibers of fasciculus gracilis and fasciculus cuneatus end at the *gracilis* and the *cuneatus* nuclei, respectively, at the lower part of medulla. The second-order neurons that originate from the nucleus gracilis and nucleus cuneatus cross to the opposite side

of the spinal cord (sensory decussation) and then they ascend as a single compact bundle called the *medial lemniscus*. This runs through the medial part of the medulla, pons, and midbrain. (It should be noted that the somatosensory evoked potentials or SSEP elicited by the electrical stimulation are primarily mediated through this posterior column-medial lemniscus system, not through spinothalamic-spinal lemniscus system. Thus, most of SSEPs are normal in patients with loss of pain-temperature sense alone.) At the pons, both the spinal and the medial lemnisci ascend together and end at the synaptic connections with the *ventral-posterior-lateral (VPL) nuclei* of the thalamus (Fig. 4-1). After synaptic connections at the VPL nuclei, the third-order fibers pass through the posterior limb of the *internal capsule* and finally end at the *primary sensory cortex (area 3b)* of the postcentral gyrus of the cerebral cortex. Similar to the motor cortex representation, the sensory area representing the upper extremities occupies a larger portion of the lateral cortex, whereas that from the lower extremities occupies the parietal and medial aspect of the cerebral hemisphere (see *Practical Guide: EEG*, Fig. 5-9).

## SOMATOSENSORY EVOKED POTENTIALS

Somatosensory evoked potentials (SSEP) can be elicited by various sensory stimuli using mechanical devices; touch,<sup>1</sup> pain, or vibration stimulation excites specific sensory receptors and will elicit modality specific SSEPs.<sup>2</sup> More recently, CO<sub>2</sub> laser stimulation has been used to stimulate pain fibers selectively.<sup>3,4</sup> Although these stimulations are more natural than electrical stimulation, their technical complexity and relatively small responses make clinical application of these nonelectrical stimulations difficult. The electrical stimulation to the peripheral nerve is technically simple and yields distinct responses along the sensory pathway. Both mixed (motor and sensory) and pure sensory nerve stimulations will evoke an SSEP of similar waveform, but the response is generally larger with mixed than with pure sensory nerve stimulation. For this reason, mixed nerve stimulations are more commonly used for clinical diagnostic tests. For upper extremity SSEP, median or ulnar nerve stimulation at the wrist is used. For lower extremity SSEP, tibial nerve at the ankle or peroneal nerve stimulation at the popliteal fossa (behind the knee) is used.



**Figure 4-1.** Anatomy of the three types of sensory pathways carrying pain and temperature (**A**), light touch and pressure (**B**), and vibration and proprioceptive sensation (**C**). The slowest-conducting fibers for pain and temperature senses cross to the opposite side after entering the spinal cord and ascend through the lateral spinothalamic tract. Light touch and pressure senses, conveyed through medium-conducting fibers, also cross to the opposite side and ascend through the anterior spinothalamic tract. The fastest-conducting fibers carrying vibration and proprioception (position sense) ascend as the dorsal column on the same side as they enter. These fibers cross to the opposite side at the medulla and ascend as the medial lemniscus. All three types of sensory fibers end in the primary sensory cortex (area 3b) of the contralateral hemisphere after synaptic connection at the VPL (Ventral-Postero-Lateral) nuclei of thalamus. (Modified from Snell RS. *Clinical Neuroanatomy for Medical Students. The Ascending Tracts of the Spinal Cord*. 5th ed. Baltimore, MD: Lippincott Williams & Wilkins, 2001:145–157, with permission.)

The SSEP consists of short-latency (<30 ms), medium-latency (30–100 ms), and long-latency (>100 ms) components. Short-latency SSEP is generally resistant to change in level of consciousness. Medium- or long-latency potentials vary depending on the patient's vigilance and various cognitive functions. Although the amplitude of short-latency SSEP is smaller than the medium- or long-latency SSEP, the stable nature of short-latency SSEP makes it more suitable for neurological diagnostic tests. Most clinical SSEP studies, therefore, have focused on short-latency SSEP, which consists of near-field as well as far-field potentials.

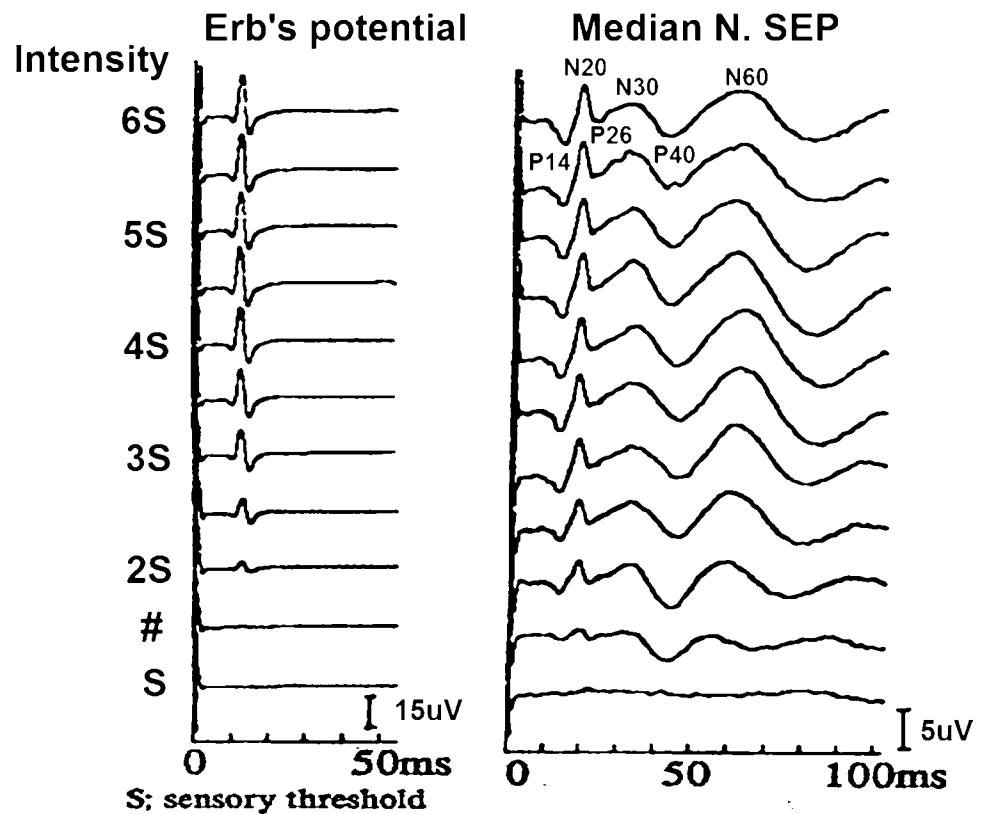
## METHODOLOGY/RECORDING TECHNIQUE

### STIMULATION

Stimulus electrodes are applied to the skin overlying the nerve to be stimulated. For upper extremity SSEP, the median or ulnar nerve is stimulated. The most commonly used electrode is a bar electrode with two imbedded electrodes, one acting as a cathode (negative pole) and the other as an anode (positive pole). The anode is placed 2 to 3 cm proximal to the distal

crease of the wrist, and the cathode is about 2 cm proximal to the anode. For lower extremity SSEP, the tibial nerve is commonly used with the stimulus electrodes at the medial aspect of the ankle; along the medial malleolus, again with the cathode being paroxysmal to the anode. These are mixed nerves containing both motor and sensory nerve fibers. Pure sensory nerves in the upper extremity can be stimulated at the fingers using ring electrodes. The sural nerve over the dorsum of the foot can be stimulated to obtain pure sensory nerve in the lower extremity. Mixed nerve stimulation is generally preferred to pure sensory nerve stimulation since the former yields responses with greater amplitude and clarity than the latter. Also, stimulus intensity is more objectively assessed by observing the resultant muscle twitch in a mixed nerve rather than relying on subjective sensory perception when using a pure sensory nerve.

Stimulus electrodes should be placed where the muscle twitch is elicited with the smallest stimulus intensity. Monophasic rectangular pulses with duration of 0.1 to 0.3 ms are delivered via a stimulus isolation unit that limits the current spread around the stimulus electrodes, reducing stimulus artifact and possible electrical hazard to the patient. Constant voltage and constant current stimulators are commercially available. Constant current stimulation is preferred because it delivers the

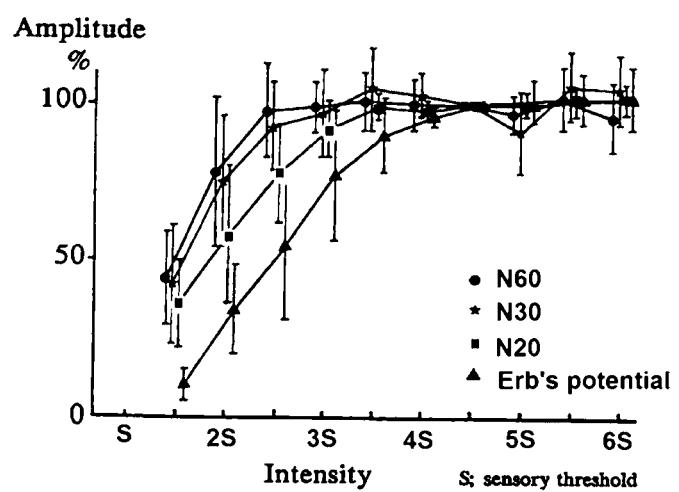


**Figure 4-2.** The amplitude changes of peripheral potential (Erb's potential) and scalp SSEP in relationship with stimulus intensity in one subject. Note that the Erb's potential reaches supramaximum amplitude at intensity between four and five times the sensory thresholds, while SSEP reaches supramaximum amplitude at intensity between three and four times the sensory thresholds.

current intensity at a set value irrespective of the electrode impedance, whereas the constant voltage stimulation delivers variable current intensity depending on the impedance of the stimulus electrode. The amplitude of scalp recorded short-latency SSEP increases linearly with increased stimulus intensity until supramaximum stimulus intensity is achieved. (Supramaximum intensity is defined as the lowest stimulus intensity above which no further increase of response amplitude is observed.) Supramaximum stimulus intensity is lower in short-latency SSEP than that in peripheral nerve action potentials (Figs. 4-2 and 4-3). It is important to deliver stimulus intensity above the supramaximum intensity for appropriate amplitude comparison of the two sets of responses. The optimal stimulus intensity is three to four times the sensory threshold (the intensity when the subject first perceives the stimulus), or 1.3 to 1.5 times the motor threshold (the intensity when the appropriate muscle begins to twitch).<sup>5</sup> The intensity generally ranges from 10 to 20 mA for constant current or from 80 to 120 V for constant voltage stimulation. Although the latencies change little with varying stimulus intensity, we found a slight shortening of latency in short-latency SSEP components with increased stimulus intensity.<sup>6</sup>

The stimulus rate is 3 to 4 Hz for recording SSEP within 50 ms after the stimulus. The rate can be increased up to 8 Hz without significantly affecting latency or amplitude of components within a 25 to 30 ms latency range in the median nerve SSEP.<sup>6</sup> The increase of stimulus rate to 10 Hz may attenuate amplitude but without changes in latency in short-latency SSEP. In lower extremity SSEP, however, we have found that increasing the stimulus rate from 2.3 to 5.1 Hz decreases the amplitude

of P40-N50 and N50-P60 components in mixed nerve SSEP, that is, common peroneal and tibial SSEPs (to a greater degree with the former than the latter) but not in pure sensory (sural) nerve SSEP.<sup>7</sup> This is explained by movement-induced interference ("gating effect") accompanied by stimulating the mixed



**Figure 4-3.** The mean amplitude changes of Erb's potential and SSEP components in relationship with stimulus intensity from 20 normal subjects. Note all three components (N20, N30, N60) of SSEP reach 100% amplitude (supramaximum amplitude) at about 3.5 times sensory threshold, while Erb's potential reaches 100% at 4.5 times the sensory threshold. Vertical lines indicate standard deviations.

nerves. A rate faster than 3 Hz attenuates components that have latency greater than 40 ms in median nerve SSEP. For the study of long-latency SSEP (>100 ms latency range), a rate slower than 0.5 Hz should be used (see Fig. 4-16).

#### FREQUENCY FILTER SETTING

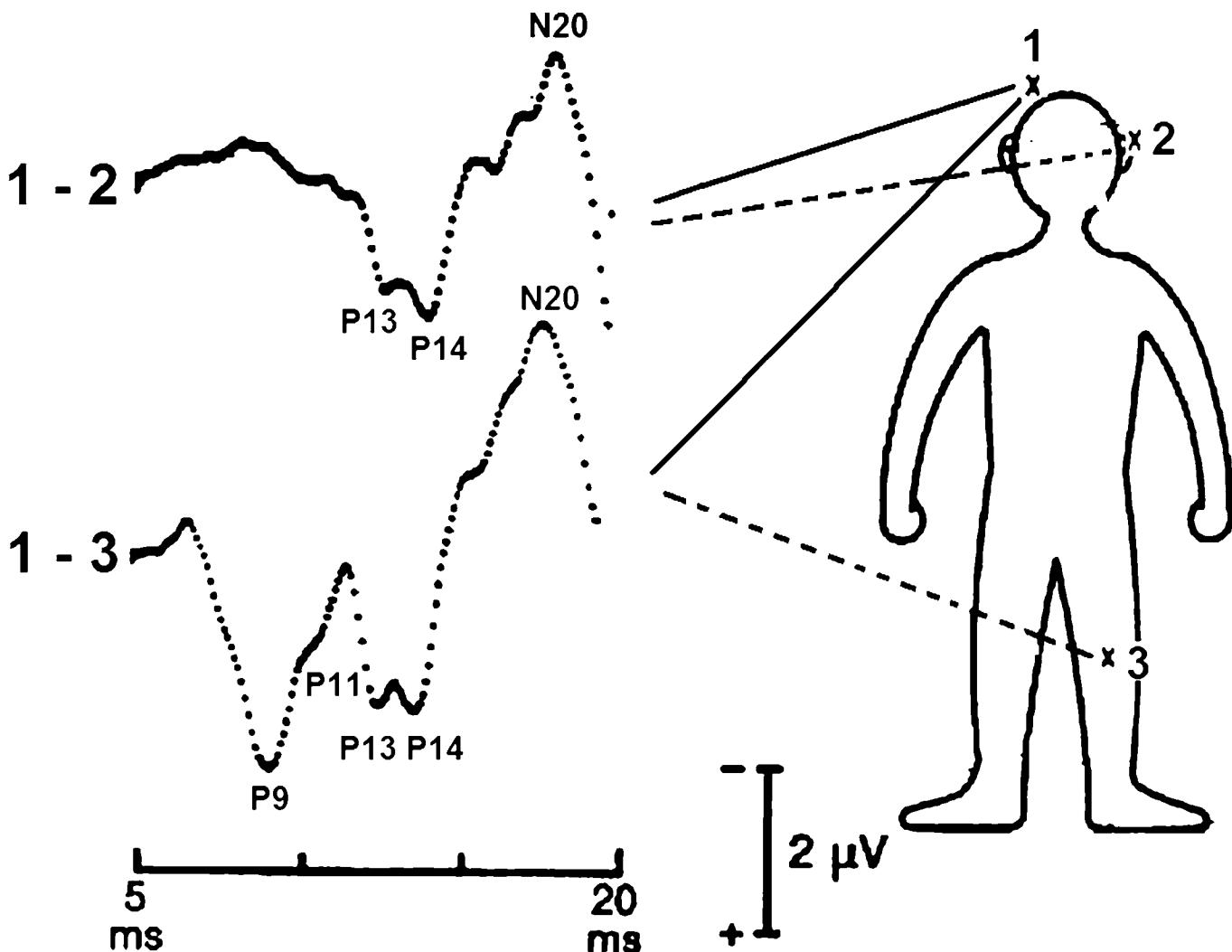
Frequency bandwidth for short-latency SSEP may vary from 5 to 30 Hz for a low-frequency filter (high pass) and 1 to 3 kHz for high-frequency filter (low pass). Theoretically, it is preferable to record with the filters wide-open (1–3,000 Hz); however, this will likely increase technical problems.

Medium- and long-latency SSEPs require a low-frequency filter lower than 5 Hz and 1 Hz, respectively. With appropriate filter settings, it is possible to enhance or attenuate a particular component of interest (see Fig. 1-16, also Fig. 4-7). The digital filtering performed offline, unlike analog filtering, causes no latency shift. The potentials measured in the digitally filtered tracing can

be correlated directly with those of the original tracing, which was recorded with a wide-open band pass filter (see Fig. 1-15).

#### AMPLIFICATION AND SUMMATION

The amplification is generally 200,000 to 500,000. Because the autorejection mode is determined by the amplitude scale, unrealistically large responses contaminated by artifact are rejected from the average. Therefore, amplification is optimally increased to reject approximately 10% to 15% of the total samples. The number of responses that are averaged should be a minimum of 1,000 responses for a short-latency SSEP, including far-field potentials. Because long-latency SSEP has much higher amplitude than short-latency SSEP, less than 100 summated responses may suffice (see Fig. 4-16). An increase in the number of summations may decrease the amplitude of long-latency components due to habituation or decreased attentiveness to the repetitive stimuli.



**Figure 4-4.** Scalp SSEPs recorded with ear and distant (knee) reference. Note P9 potential recorded with knee reference is absent when an ear reference is used. The absence of P9 with ear reference is due to equipotential activity between scalp and ear electrodes indicating P9 is a widespread potential. (From Yamada T, Kimura J, Nitz DM. Short latency somatosensory evoked potentials following median nerve stimulation. *Electroencephalogr Clin Neurophysiol* 1980;48:367–376, with permission.)

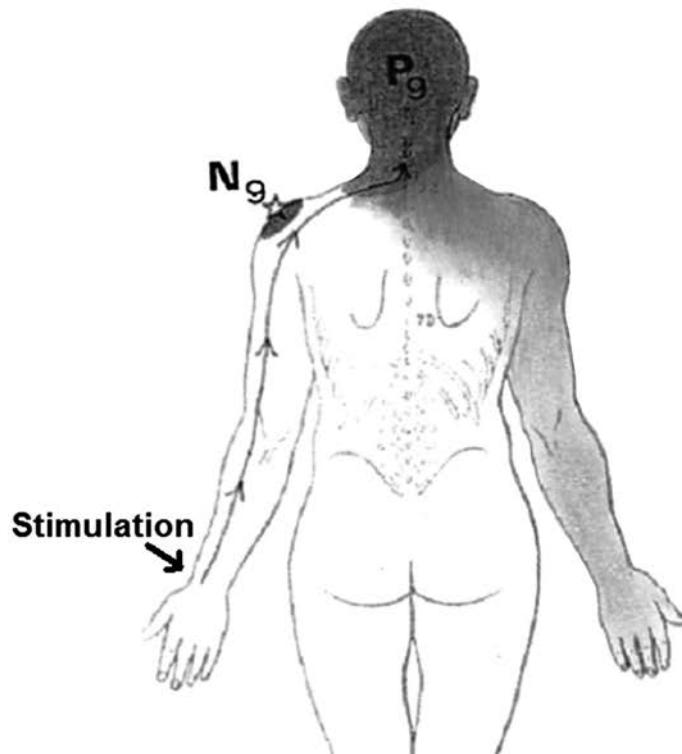
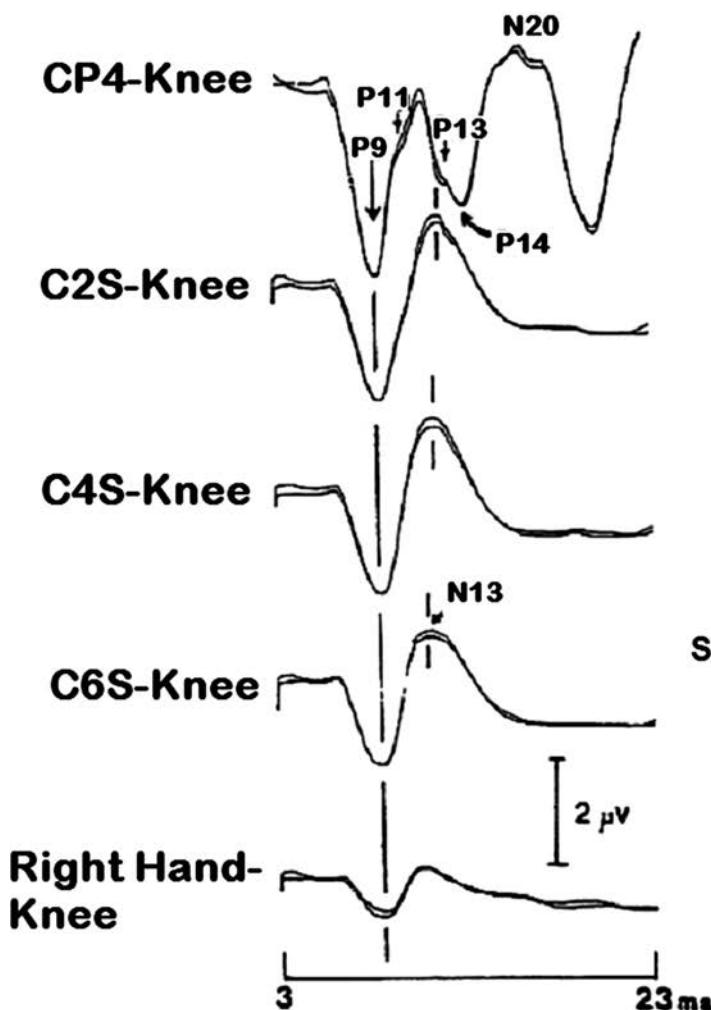
## GENERATION MECHANISM OF FAR-FIELD POTENTIAL (FFP)

Although the concept of FFP was first introduced in brainstem auditory evoked potentials (BAEP),<sup>8</sup> its generation mechanism has been explored more extensively in SSEP. FFPs are potentials recorded at a distance from the neural generators. Because the FFPs have a wide field distribution, conventional bipolar recording with short interelectrode distance cancels out the FFP due to equipotentiality between the two electrodes. FFPs are recorded only when the distance between the two electrodes is sufficiently great such that an amplitude difference exists between the two electrodes. Conversely, short distance, bipolar electrode pairs cancel out FFP and record only localized, near-field potentials (NFP) (generated near the recording electrodes). A mixture of FFP and NFP in SSEP increases the complexity of the SSEP. However, adding the FFP recording increases the clinical utility of the SSEP by detecting subcortical potentials

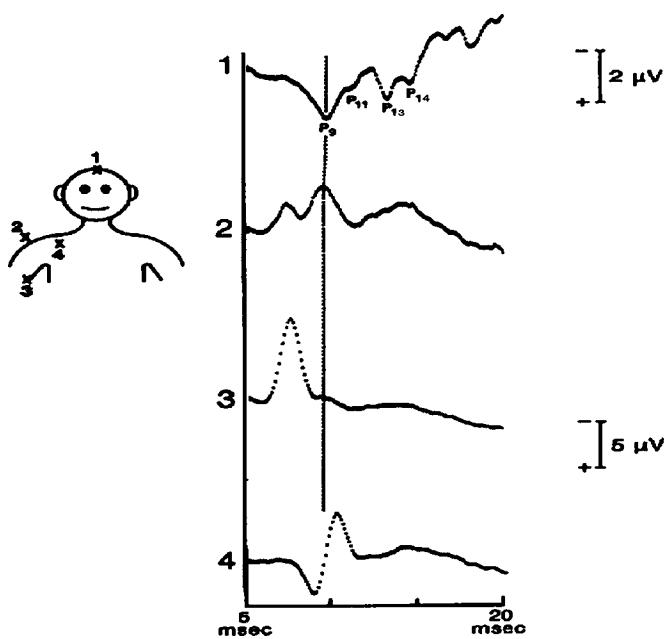
that are not otherwise accessible by conventional surface recording.

An example of FFP recording is shown in Figure 4-4. Following median nerve stimulation at the wrist, the initial large positive potential (P9) is recorded from the scalp with a distant (knee in this case) reference but not with the ear as reference. This is because the P9 potential is widely distributed over the entire scalp including the ears. In fact, P9 can be recorded even on the contralateral hand (Fig. 4-5). Equipotential activity in the scalp with an ear reference will result in the cancellation of P9. The latency of 9 ms is theoretically too short for a traveling impulse from the wrist to reach the cortex (scalp electrode), unless the conduction velocity is unrealistically fast. This implies that the P9 potential reflects activity generated at a distance from the electrode location, that is, the scalp. The question is, then, where P9 is generated. Recording the peripheral nerve potentials (traveling impulse) from the proximal arm to the shoulder revealed that a negative

## Left Median N. Stimulation



**Figure 4-5.** Field distribution of P9 FFP. P9 can be recorded from a wide area of the body extending from the scalp and neck to the hand contralateral to the side of stimulation with gradual decreasing amplitude.



**Figure 4-6.** The latency relationship between P9 and peripheral nerve action potential. P9 latency is slightly longer than the negative peak of the action potential at the axilla (3) and slightly shorter than the Erb's potential (4). P9 latency matches the negative peak of the potential recorded at the acromion (2). (From Yamada T, Kimura J, Nitz DM. Short latency somatosensory evoked potentials following median nerve stimulation. *Electroencephalogr Clin Neurophysiol* 1980;48:367-376, with permission.)

peak (N9) recorded at the acromion best matched the P9 latency, indicating that P9 arises from the distal portion of the brachial plexus, slightly distal to the Erb's point (Fig. 4-6). The next question is, then, why the FFP is generated as the nerve impulse passes through a certain and fixed anatomical site. Earlier studies of BAEP proposed that the FFPs of waves II through V were generated when the impulse passed through each synaptic site of the brainstem auditory pathway. However, in the P9 model of SSEP, there is no synaptic connection at this shoulder area (the first synaptic connection in the ascending sensory pathway is at the dorsal root ganglion, close to the entrance to the spinal cord). Therefore, the synaptic theory does not explain the generation of FFP. The major change occurring at the shoulder area is the change of volume surrounding the nerve, that is, the traveling impulse suddenly enters from the small (arm) to large (body) volume area (see Fig. 4-5). This suggests that the axonal volley (not synaptic discharges) generates the FFP when the volume conduction surrounding the nerve suddenly changes.

In addition to the concept that a sudden change of volume conductive media surrounding the nerve generates the FFPs,<sup>9</sup> two other generation mechanisms have been proposed: one of the mechanisms states that the FFPs are generated whenever the impulse passes through a different conductivity or compartment surrounding the nerve.<sup>10</sup> The other mechanism is the change of the direction/orientation of the nerve impulse. This was proposed by the finding that changing the arm position altered waveforms and latency of the P9 FFP.<sup>11-13</sup> All three of the above mechanisms for generation of FFPs were supported by computer simulation models.<sup>14</sup>

The early definition of FFP was a positive polarity reflected by the advancing positive field when the impulse is approaching the recording electrode. Recent studies, however, demonstrated that FFP may be either positive or negative depending on the location of electrodes in respect to the orientation of the dipole generator.<sup>15</sup> The complexity of human geometry and inhomogeneous conductivity, and a nonstraight pattern of nerve pathway could create infinite possibilities of FFP having many varieties of characteristics and distribution.

## PHYSIOLOGICAL FACTORS THAT AFFECT SSEP

### AGE

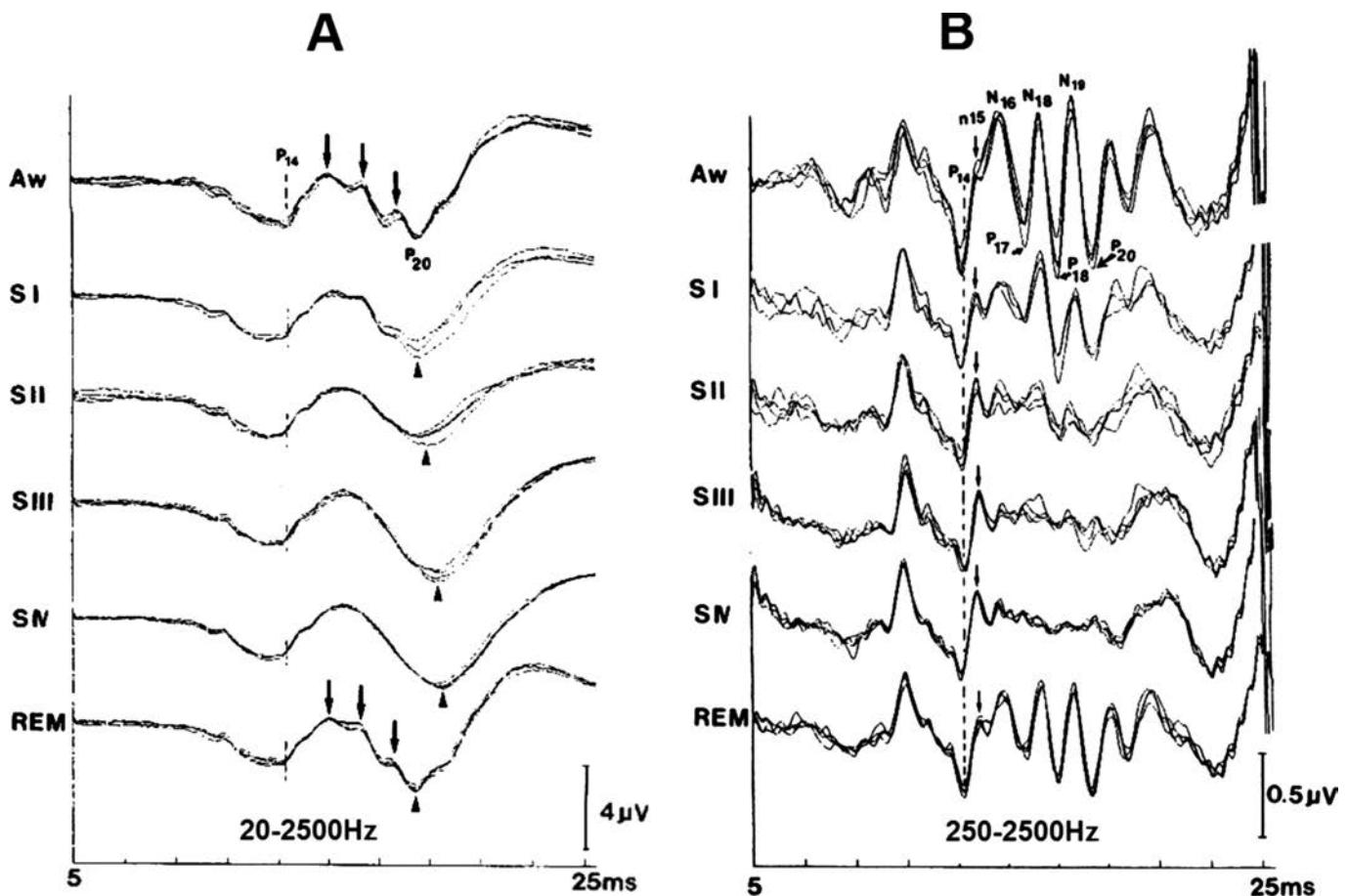
Latency is dependent upon the peripheral-central conduction velocity and height (for lower extremities) or arm length (for upper extremity) (see Appendix Figs. 4A-1 to 4A-12). Peripheral conduction velocities reach adult levels by age 3 and spinal conduction velocities by age 5.<sup>16,17</sup> The latency differences after this age are primarily a result of height or arm length. Generally, the latency stays stable from the late teens to 50 years of age with a small increase (0.3 ms) after the age of 50.<sup>18</sup>

In infants and children, the latency changes are secondary to the combined effects of maturation of peripheral and central somatosensory pathways, and the increase in these pathways along with body growth. With the combined effects of maturation and increasing body size, the latencies of Erb's potential and the cervical response remain relatively unchanged from birth to 2 or 3 years of age and then increase to adult levels by 14 to 19 years.<sup>19</sup> Because myelination of the peripheral fibers progresses faster than that of the central pathways,<sup>20</sup> the interpeak latency (IPL) between cervical N13 and cortical N20 (central conduction time) progressively decreases until about 6 to 7 years of age, whereas the IPL between Erb's potential and cervical N13 remains constant.<sup>21,22</sup> For example, the N13-N20 IPL at birth is about 10 to 11 ms and decreases to the adult value (7 ms) by 6 to 8 years of age. Erb's potential—N13 IPL remains at about 3 ms until about 3 to 4 years. This is about 1 ms shorter than the adult value, presumably due to the small body size.

Before the age of about 5 years, cortical components by upper and lower extremity stimulation have a broader duration. Overall waveform morphology becomes similar to adults after the age of 5.<sup>23,24</sup>

### BODY SIZE

After myelination is complete and the conduction velocity of the sensory pathway is established (around the age of 3–4 years), the absolute latency values correlate linearly with the arm length or height, that is, distance between stimulus site and waveform generator.<sup>25,26</sup> If absolute latencies are used for interpretation, it is necessary to correlate them with the arm length for an upper extremity study and height for a lower extremity study (see Appendix Figs. 4A-1 to 4A-12). If, however, IPLs are used, for example Erb's potential to N13 or N13 to N20 for upper extremity and N23 (spinal potential) to P37 (P40) for lower extremity, the effect of differences in body size is small enough and can be ignored in the adult population for clinical application.



**Figure 4-7.** Changes of high-frequency oscillation (HFO) from awake to sleep. Note there are small wavelets over the frontal negative potential that are most prominent in awake and disappear in non-REM (stage 1 through 4 sleep), and recover some in REM sleep (**A**). Raising the low filter from 20 to 250 Hz with a digital filter shows clear differences of these HFO between the awake state and non-REM sleep (**B**). (From Yamada T, Kameyama S, Fuchigami Y, et al. Change of short latency somatosensory evoked potential in sleep. *Electroencephalogr Clin Neurophysiol* 1988;70:126-136, with permission.)

## TEMPERATURE

Lowering the limb temperature significantly increases the peripheral nerve conduction velocity. For example, P37 (P40) (cortical potential) after tibial nerve stimulation is prolonged by 1.15 ms with 1°C of temperature decrease.<sup>27</sup> An increase of body temperature has less effect in SSEP latencies.<sup>28,29</sup> The accepted protocol used in the EMG laboratory should be applied to SSEP testing in order to avoid interpretation errors due to deviations from normal body/limb temperature (see Chapter 16, page 286, "Temperature").

## SLEEP

Sleep has little effect on short-latency far-field potentials but significantly alters medium- (40–100 ms) and long-latency (>100 ms) components. The medium-latency components, for example, N60 of median nerve SSEP shows latency prolongation and amplitude reduction. Long-latency components totally disappear (see more detail on page 64, "Medium and long latency SSEPs after upper extremity stimulation" and also Fig. 4-17). The first cortical potential in median nerve SSEP, N20, was earlier thought not to be affected by sleep, but detailed

studies have found that N20 latency prolongs slightly in deep sleep.<sup>30,31</sup> However, the latency prolongation in stage I or II sleep is minimal; thus, it can be ignored during routine clinical testing. Detailed analysis of N20 has shown multiple fast components (400–600 Hz) superimposed over the N20 waveform. These fast-frequency components (commonly referred to as *high-frequency oscillation* or *HFO*) are best recognized in wakefulness and disappear in non-REM sleep but reappear in REM sleep (Fig. 4-7).<sup>31,32</sup> In recent years, there has been increasing interest in HFOs in relationship to clinical correlates as well as physiological significance.<sup>33–36</sup>

## SHORT-LATENCY UPPER EXTREMITY SSEP

Description in this section will mainly focus on median nerve SSEP since it is the most commonly used nerve in upper extremity SSEP. Ulnar nerve stimulation at the wrist elicits a similar response, but with slightly smaller amplitude and slightly longer latency. Short-latency SSEP consists of FFPs and NFPs. Depending on the electrode derivations, a certain potential can be

enhanced or eliminated, and expressed as an upward or a downward deflection.<sup>37-39</sup> Knowledge of polarity and field distribution of each component is, therefore, important to understand the rationale of chosen electrode derivations and montages.

In order to record FFPs, a noncephalic reference must be used as was discussed earlier in this chapter. Scalp electrodes referred to a noncephalic reference register FFPs of P9, P11, P13, and P14 (see Fig. 4-4). The reference electrode can be placed at the contralateral shoulder (Erb's point), hand, or knee. Although some FFPs, for example P9, have higher amplitude when the reference electrode is further away from the head, the use of very long interelectrode distances encounters more technical problems such as an increase in stimulus artifact, sample rejection, and muscle or movement artifacts. A commonly used noncephalic reference is the Erb's point contralateral to the side of stimulation. Though P9 is partially canceled with this reference, it is recordable because there is sufficient amplitude difference between the scalp and the reference electrodes.

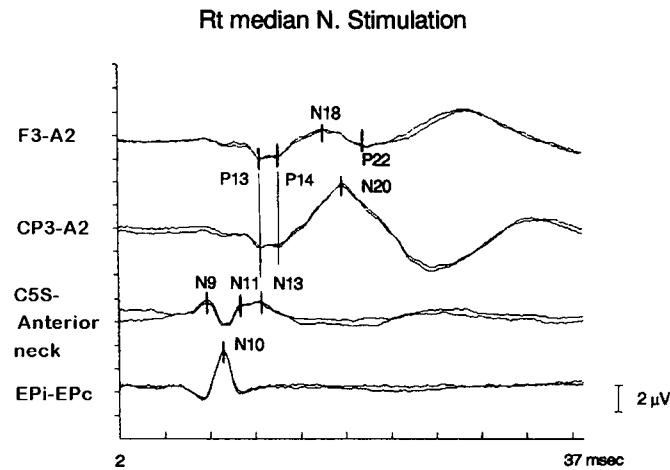
When referenced to the ear, P9 and P11 potentials are canceled out due to equipotentiality of these peaks between scalp and ear electrodes (see Fig. 4-4). P13 and P14 are also FFPs but their distributions are more limited, not involving the ear; thus, they can be recorded with the ear reference.

### P9 AND N9 POTENTIALS

P9 is distributed widely from the scalp, neck, and to the hand contralateral to the side of stimulation, with gradually decreasing amplitude rostrally (see Fig. 4-5). The peak latency is slightly longer than the negative peak of Erb's potential and matches the negative potential recorded at the acromion (see Fig. 4-6). Therefore, it has been agreed that P9 is generated at the distal portion of brachial plexus.<sup>11,39</sup> This P9 potential is recorded as "N9" in the derivation of posterior neck (C5S)-anterior neck (AN) (Fig. 4-8; see also Fig. 4-13B) or posterior neck-ear derivation due to a greater positivity at the anterior neck or ear than the posterior neck (C5S) electrode.

### P11 AND N11 POTENTIALS

Cervical P11 is much smaller than other far-field potentials and may not be consistently recorded in normal subjects. It is distributed over the entire scalp and spreads to the high cervical region. P11 latency matches the small negative peak (N11) recorded at the low cervical (C5S) spine and is slightly later than the small negative notched wave recorded at the lateral neck on the side of stimulation (Fig. 4-9). The latency of 11 ms is close to the estimated conduction time of a nerve impulse arriving at the cervical spine, and therefore P11 is considered to be a presynaptic potential generated at the root entry zone.<sup>38-41</sup> When a cervical electrode is referenced to the scalp or to the ear (this was one of the derivations recommended earlier by the American EEG Society in 1984<sup>42</sup>), N11 is accentuated because of an additive effect with P11 from ear or scalp electrodes. Although this derivation effectively accentuates N11, it is no longer recommended because it results in an amalgam of N13 (cervical) and P13/P14 (scalp) peaks that have different anatomical origins (see more details in the next section), and as a consequence this derivation fails to



**Figure 4-8.** 4-channel SSEP recording after right median nerve stimulation. F3 (Fc) registers P13, P14, and N18 FFPs and CP3 (CPc) registers P13 and P14 FFPs, and N20 (first cortical potential). C5S (cervical spine electrode) shows N9, N11, and N13. The negative peak of Erb's potential (N10) occurs between N9 and N11. (Modified from Yamada T. Somatosensory evoked potentials In: Weinstein SL, ed. *The Pediatric Spine: Principles and Practice*. New York, NY: Raven Press, 1994: 1171-1179, with permission.)

distinguish cervical and brainstem components. N11 is usually recognized as a small notch on the rising phase of N13 in a C5S (posterior neck)-AN (anterior neck) derivation (see Fig. 4-8 and also 4-13B).

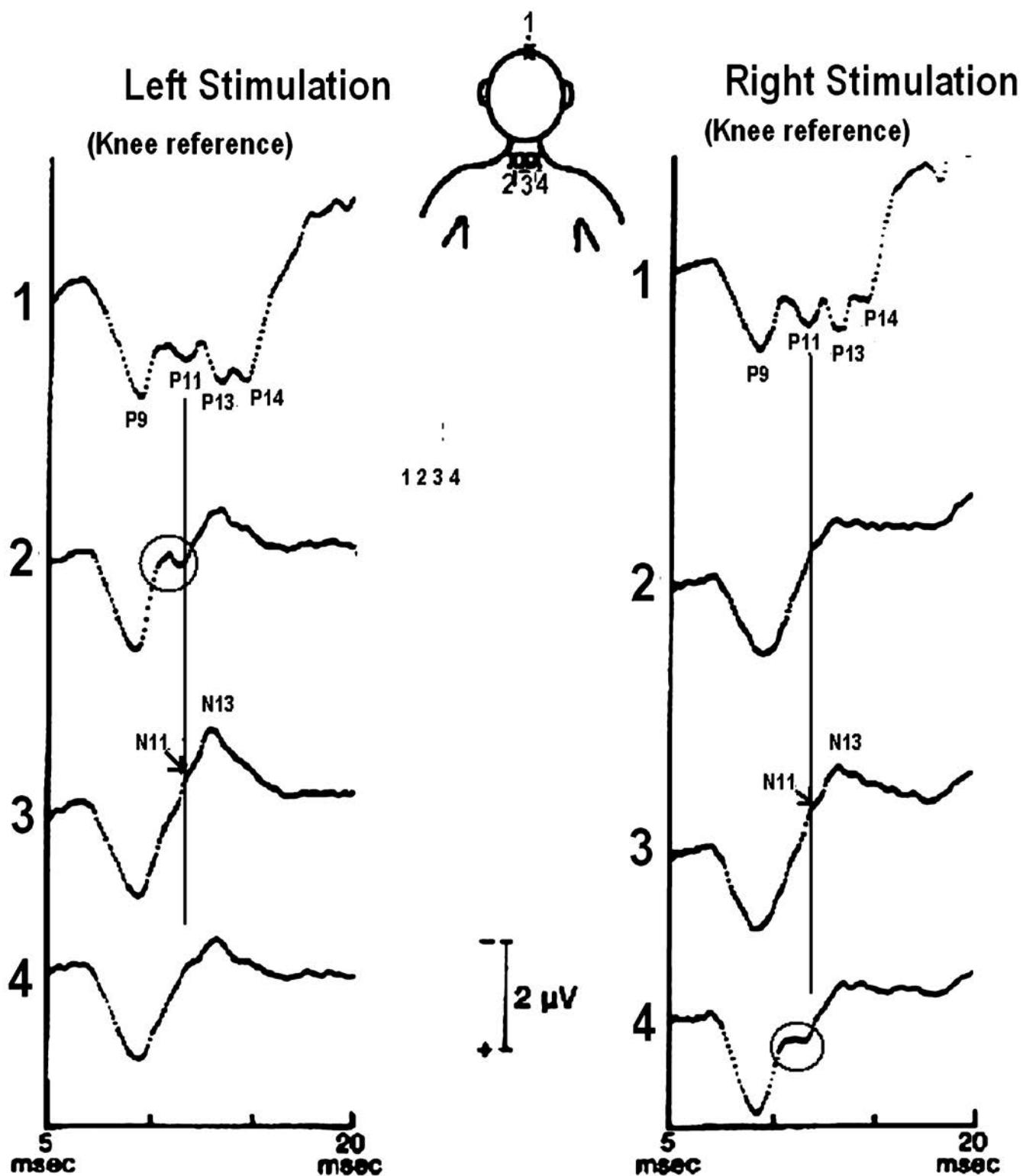
### P13/P14 POTENTIALS

P13 and P14 potentials often appear as a bifid positivity, though the bifid configuration may not always be distinct. P14 is measured at the onset of the rising negativity of N18 or N20 (see Figs. 4-8 and 4-10).

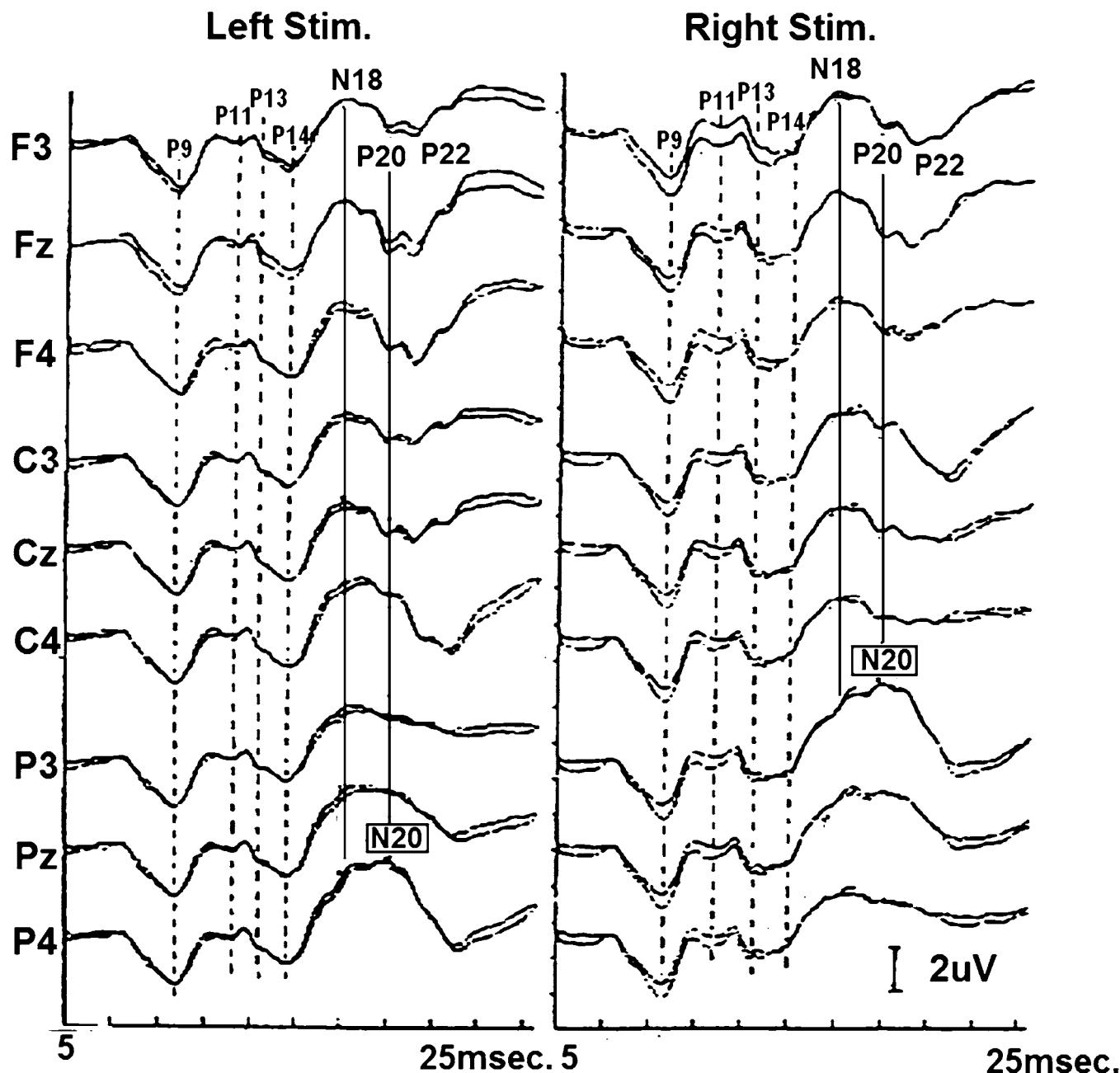
In contrast to P9 and P11, which are widely distributed over the entire head and neck, the distribution of P13/P14 is limited to the crown of the scalp. Therefore, unlike P9 and P11, P13/P14 can be recorded with an ear reference (see Figs. 4-4, 4-8, and 4-10) because P13 and P14 are less active at the ear than the scalp. Although P13/P14 have generally been regarded as complex and are thought to originate from the medial lemniscus, their origins are likely to be separate generators<sup>43,44</sup> as will be described more in relationship with "cervical potential".

### N18 POTENTIAL

Like P13/P14, N18 is also widely distributed over the crown of the scalp and can be recorded over the bifrontal region and ipsilateral hemisphere using an ear reference (Fig. 4-10). N18 is also present at the contralateral postcentral (CP) electrode, often as a small notch over the rising phase of N20 (Figs. 4-10 and 4-11). This is a relatively slow potential having long duration (see Figs. 4-32 and 4-34) and can be enhanced when a low filter of less than 5 Hz is used. Because of its wide distribution, N18 is also considered to be an FFP. Earlier studies thought it arose from the thalamus,<sup>45,46</sup> but later studies suggest a more caudal origin of N18, either at the pons or at the medulla.<sup>47,48</sup>



**Figure 4-9.** The relationship between P11 FFP and N11 (cervical) response. Note P11/N11 latency is slightly longer than the negative notched wave (shown in the circle), which appears only on the stimulated side. This notched wave likely represents the impulse just before the entrance to the spinal cord. This is consistent with the notion that N11/P11 arise from the root entry zone. (From Yamada T, Yeh M, Kimura J. Fundamental principles of somatosensory evoked potentials In: Lew HL, Kraft GH, eds. *Physical Medicine and Rehabilitation Clinics of North America*. vol. 15. Philadelphia, PA; Elsevier Saunders, 2004:19–42, with permission.)



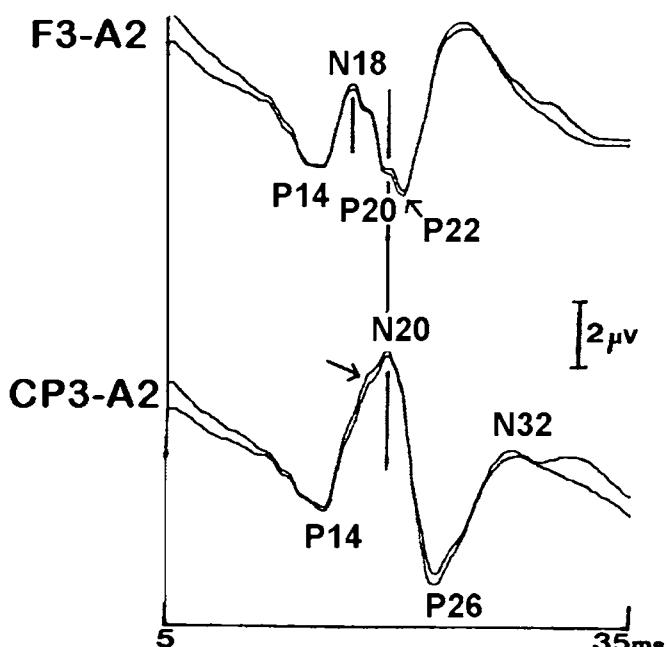
**Figure 4-10.** Characteristic field distribution of various SSEP components. P9, P11, P13, and P14 FFPs are evenly distributed over the entire scalp. N18 FFP is also widely distributed and can also be seen as a small notched wave over the rising phase of N20 at the contralateral parietal electrode. Frontal P20 and parietal N20 show an inverted phase relationship implicating a dipole field distribution. Note there is another positive peak (P22) following P20 at the frontal electrode. (From Yamada T. The anatomic and physiologic bases of median nerve somatosensory evoked potentials. In: Gilmore R, ed. *Neurologic Clinics*, vol. 6. Philadelphia, PA: WB Saunders Co. 1988:705–733, with permission.)

#### N20, P20, P22 POTENTIALS

N20 (cortical potential) is the first NFP (near-field potential) following the FFPs. It is localized to the postcentral electrode on the contralateral hemisphere (see Fig. 4-10). The postcentral electrode is usually applied half way between the central and parietal electrodes (CP). N20 negativity often shows a notched configuration over its rising phase that corresponds to N18 recorded from the bifrontal or ipsilateral CP electrode (see Figs. 4-10 and 4-11). N20 latency closely matches P20 recorded from

the frontal electrode (see Figs. 4-10 and 4-11). This parietal N20 and frontal P20 relationship has been considered to be a horizontally oriented dipole directed tangentially from the parietal to the frontal region<sup>49–51</sup> (Fig. 4-12). Indeed, direct cortical recording shows a polarity inversion across the central sulcus; that is, N20 at the postcentral primary sensory cortex and P20 at the precentral motor cortex (see Chapter 5, Fig. 5-5). Because of this dipole relationship between N20 and P20, both presumably arising from the same generator, earlier studies used the CP elec-

## Rt. Median N. Stimulation



**Figure 4-11.** Relationship between frontal and parietal responses. Note phase reversal between parietal N20 and frontal P20. There is an additional positive potential P22 that is independent from frontal P20 and parietal N20. There is a small notched peak on the rising phase of N20 (indicated by arrow), which corresponds to the frontal N18. This indicates that the parietal N20 includes the N18 potential.

trode referenced to the frontal electrode (Fz) that effectively enhanced the N20 amplitude by the contribution of P20 from the frontal electrode. This was also recommended by the American EEG Society.<sup>42</sup> However, growing evidence indicates that the frontal positivity includes another component (P22) that is independent from the dipole positivity reflected by CP-N20 (see Figs. 4-10 and 4-11).<sup>52,53</sup> It has been proposed that P22 originates from the supplemental motor cortex.<sup>50,52,53</sup> Referencing to the frontal region thus creates an amalgam of two independent components that arise from separate generators. The American Clinical Neurophysiology Society (formerly The American EEG Society) guidelines, therefore, no longer recommend the use of Fz or Fpz as a reference.<sup>54</sup> The contralateral CP (CPc) electrode should be referenced to a noncephalic or an ear lobe electrode. Alternatively, a new guideline recommends CPc-CPi that yields a “pure” near-field potential, N20, by canceling out N18 and all other FFPs as they are common to both electrodes (“c” and “i” refer to the electrodes of contra- and ipsilateral hemispheres, respectively in relationship with stimulus side).<sup>54</sup> The guidelines also recommend an additional recording from CPi referenced to a noncephalic electrode, which registers only the far-field potentials of P9, P11, P13/P14, and N18 (Fig. 4-13A).

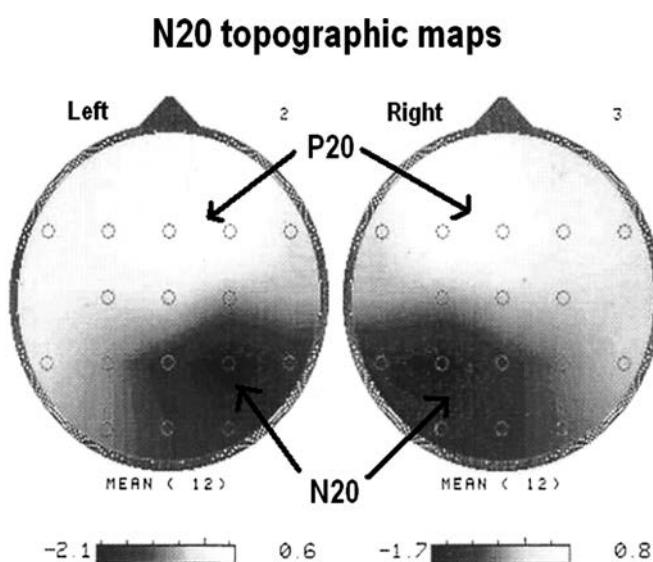
An alternative derivation is to use Fc and CPc, both referenced to the ear (linked ears or ipsilateral ear). Fc registers P13/P14, N18 and P20/P22, and CPc registers P13/P14 and N20 (Fig. 4-13B). The relationship between these two derivations can assist in peak identification; P13/P14 should be present on both derivations and N20 from CPc electrode should show near-phase reversal with P20/P22 from the Fc electrode. Also, the N20 latency of CPc should be slightly longer than N18 of the Fc electrode.

## CERVICAL RESPONSES

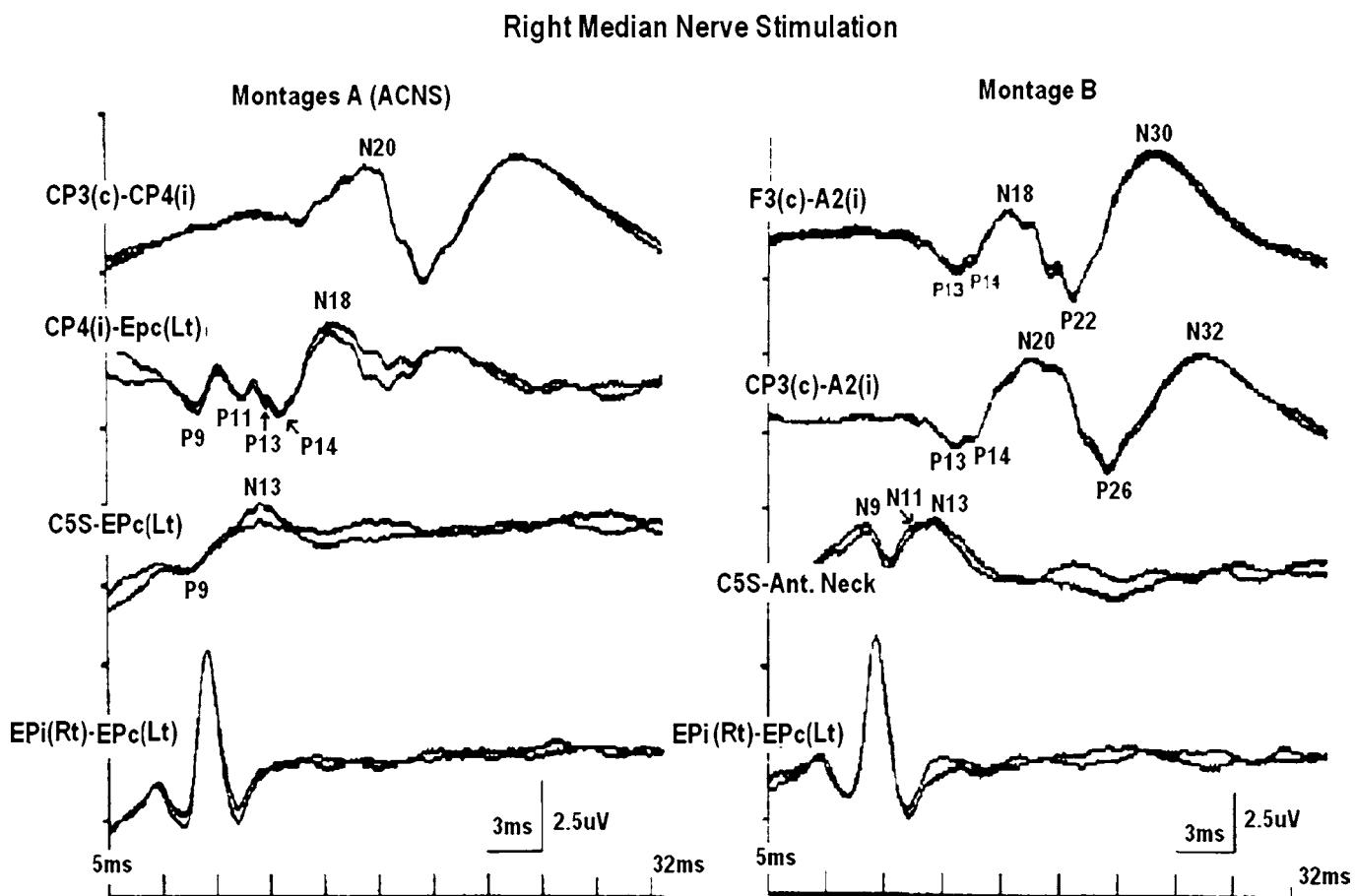
The cervical response is usually recorded either from C5S or C2S spine (5th or 2nd cervical vertebra). Either recording shows a similar negative wave with a latency of about 13 ms (N13) and duration of 200 to 300 ms (Fig. 4-14). But the latency is slightly longer at C2S than at C5S. Whether to record at C2S or at C5S has been randomly decided depending on the laboratory's preference. Recent studies, however, have indicated separate generators of N13 from C2S and C5S.<sup>55-57</sup>

### N13 Recorded from C5S

Since N13 latency closely matches P13 (FFP recorded from the scalp) (see Figs. 4-8, 4-9, 4-13, and 4-14), earlier studies thought P13 represented a vertically oriented positive dipole field generated by N13 (cervical). But it is now believed that the positive dipole field for N13 exists at the anterior neck, creating a horizontally oriented dipole (see Fig. 4-14).<sup>57,58</sup> Indeed, there have been a number of experimental and clinical studies to support this notion.<sup>59,60</sup> If the anterior neck P13 and the posterior neck N13 have the same origin, there is justification for the cervical electrode to be referenced to the anterior neck, which tends to enhance N13 (see Fig. 4-13B). When C5S is referenced to the contralateral Erb's point, the waveform consists of P9 and N13 (see Fig. 4-13A). When referenced to the anterior neck, P9 becomes “N9” because of a greater positivity at the anterior than at the posterior (C5S) neck (see Fig. 4-13B).



**Figure 4-12.** Topographic mapping of N20 distribution. Note the maximum negative (N20) field at the contralateral parietal electrode and associated frontal positive (P20) field. This represents a dipole field distribution with negativity at the parietal and positivity at the frontal regions. The bar scales at the bottom indicate a range of amplitude in  $\mu$ V.



**Figure 4-13.** A, B: Representative 4-channel montage recommended by the ACNS (A) and alternative montage (B).

The origin of N13 (C5S) was earlier thought to be the dorsal column, dorsal root, or cuneate nucleus. More recent studies, however, indicate that N13 reflects activity of the *dorsal horn interneurons* located close to the central gray matter.<sup>59,60</sup> Unlike other SSEP components that are mediated through the dorsal column-medial lemniscus system, N13 (C5S) is independent from this pathway. In support of this view, an absent N13 (C5S) with concomitant normal P13/P14 and N20 has been reported in patients with syringomyelia having impaired pain/touch but normal proprioceptive sensations<sup>61,62</sup> (see Fig. 4-27). Inter-peak latency from cervical N13 to cortical N20 can be used as a central conduction time without consideration of arm length or peripheral conduction time (see Appendix Fig. 4A-7.)

#### N13 Recorded from C2S

N13 recorded from C2S has similar or slightly longer latency than N13 at C5S (see Fig. 4-14), but recent studies have shown that these two have separate origins.<sup>55-57</sup> While C5S-N13 arises from a structure not related to the dorsal column, C2S-N13 may represent the ascending dorsal column volley reaching the cuneate nucleus. It is possible that C2S-N13 is a presynaptic potential before the cuneate nucleus.<sup>63</sup> The scalp recording FFP, P13, may indeed reflect C2S-N13 (see Fig. 4-14). Abnormal C2S-N13 in association with normal C5S-N13 has been reported in patients with high cervical cord lesions.<sup>64</sup> Recording responses from C2S and C5S, both referenced to a noncephalic site, may be useful in these cases.

#### RECORDING MONTAGES FOR SHORT-LATENCY SSEP OF UPPER EXTREMITY NERVES

It is important to understand the field distributions and physioanatomical correlates of short-latency SSEP in order to create appropriate montages. The American Clinical Neurophysiology Society (ACNS)<sup>54</sup> recommends the following four channel montages: (see Fig. 4-13A).<sup>54</sup>

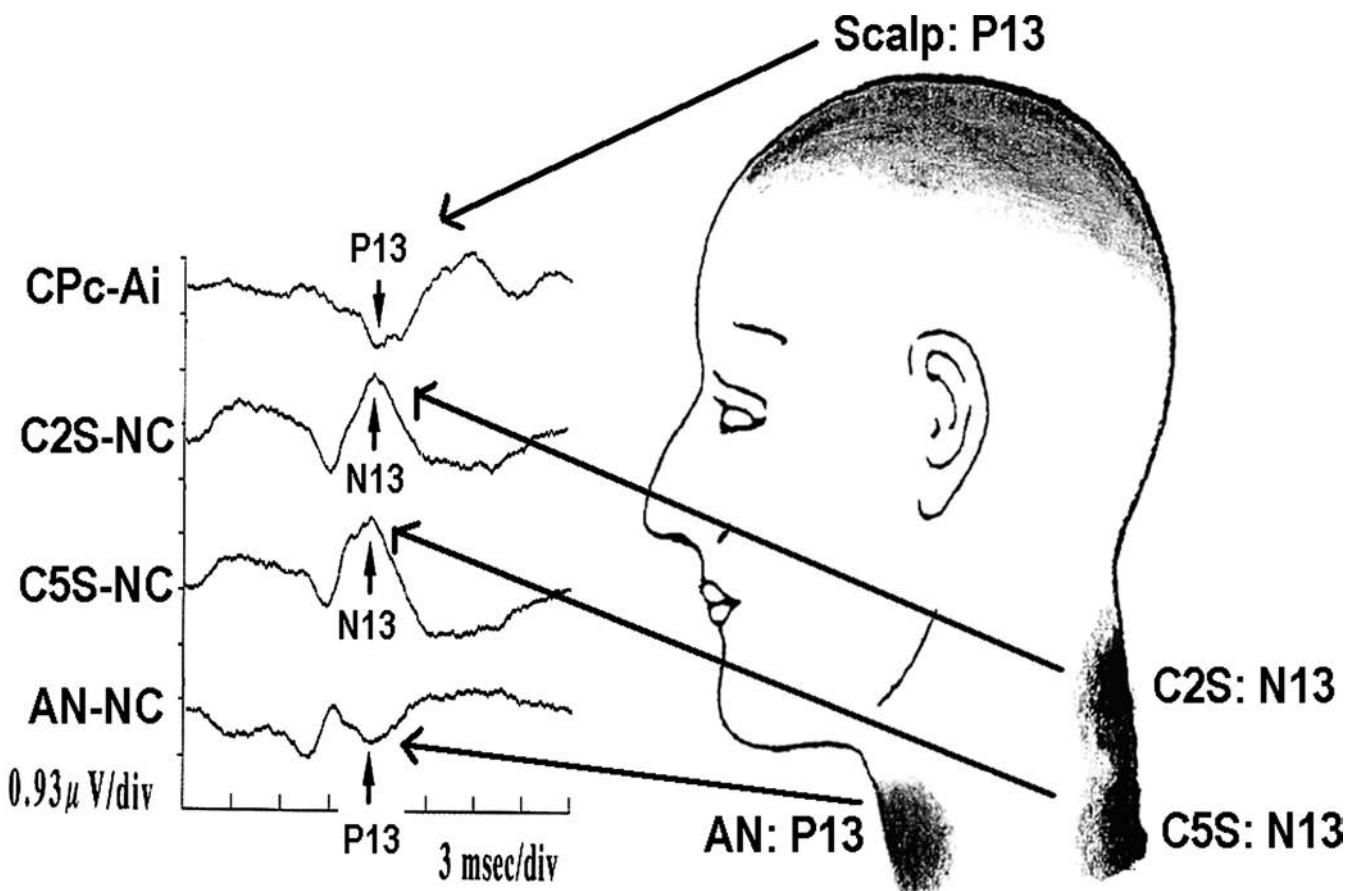
Channel 1: CPc – CPi (N20)

Channel 2: CPi – Noncephalic reference (P9, P11, P13/14, N18)

Channel 3: C5S – Noncephalic reference (P9, N13)

Channel 4: EPi – Noncephalic reference (N10)

CPc is the contralateral electrode placed halfway between central (C3, C4) and parietal (P3, P4) electrodes. CPi is the ipsilateral electrode placed halfway between central and parietal electrodes. C5s is the cervical electrode placed just above the C5 spinous process that can be estimated by finding the most prominent C7 spinous process at the base of the neck. EPi is Erb's point (just above the midpoint of the clavicle) ipsilateral to the side of stimulation. Noncephalic reference can be EPc (Erb's point contralateral to the side of stimulation) or other distant site such as hand, arm, shoulder of nonstimulated side or knee.



**NC=Non cephalic reference at hand contralateral to the side of stimulation**

**Figure 4-14.** The relationship of scalp-P13 and anterior neck-P13 vs C2S (high cervical) and C5S (low cervical) N13. It is likely that P13 (anterior neck) and N13 (C5S) reflect a horizontally oriented dipole, while P13 (scalp) and N13 (C2S) represent a vertically oriented dipole.

#### Rationale for the Above Montage

Both CPc and CPi electrodes contain P9, P11, P13/P14, and N18 FFPs but only CPc includes the near-field potential of N20 (first cortical potential). Channel 1, CPc-CPi, thus cancels all FFPs and registers only N20. Channel 2 records all FFPs (P9, P11, P13/P14, and N18) only. Channel 3 registers P9 FFP and N13 (cervical potential), and channel 4 records Erb's potential (N10).

An alternative montage is as follows (see Fig. 4-13B)

Channel 1: Fc - Ai (P13/14, N18, P20/22)

Channel 2: CPc - Ai (P13/14, N18, N20)

Channel 3: C5S - Anterior neck (N9, N11, N13)

Channel 4: EPi - EPc (N10)

*Fc is F3 or F4, contralateral to the side of stimulation. Ai is the ear reference ipsilateral to the side of stimulation. EPi and EPc are Erb's point ipsilateral and contralateral, respectively.*

#### Rationale for the Above Montage

Channel 1 registers P13/P14 and N18 FFPs and P20/P22 potentials.

Channel 2 registers P13/P14 FFPs and N20 (cortical potential) that includes N18 FFP often appearing as a small

notch over the rising phase of N20 (see Figs. 4-8, 4-10, and 4-13B). Channel 3 registers N9, N11, and N13 potentials. Of these, N9 is derived from P9 FFP. This becomes a "negative" potential because of greater positivity at anterior neck than posterior neck (CS5). Channel 4 records the Erb's potential.

The various relationships between these derivations aid in identifying multiple SSEP components accurately. P13/P14 FFPs can be identified by finding at both channels 1 and 2. These 2 channels also help to distinguish N18 FFP and N20 cortical potential by their latency difference between channels 1 and 2. Also, N20 shows a near-phase inversion with the frontal P20/P22. Channel 3 registers N9 and N11 in addition to cervical N13. Recording N9 and N11 with this derivation is technically easier than P9 and P11 FFP recording using a noncephalic reference. Moreover, cervical N13 is better defined with the anterior neck reference than with the noncephalic reference because of an additive effect of P13 from the anterior neck in the former derivation (compare Fig. 4-13A and B). The relationship between channels 3 and 4 helps to identify N9 and N11 by finding the negative peak of Erb's potential (N10) occurring between N9 and N11.

The summary of these short-latency median nerve SSEP components in relationship with anatomical origin is shown in

<b>TABLE 4.1 SSEP Components</b>		
<b>A. Median Nerve SSEP</b>		
<i>Components</i>	<i>Origin</i>	
N9/P9	Distal portion of brachial plexus	
N10	Erb's point	
N11/P11	Root entry zone	
N13	Cervical cord (dorsal horn interneuron)	
P13/P14	High cervical cord/brainstem (medial lemniscus)	
N18	Brainstem	
N20	Cortex (area 3b, postcentral gyrus)	
P26	Cortex	
<b>B. Tibial Nerve SSEP</b>		
<i>Components</i>	<i>Origin</i>	
N8	Popliteal fossa	
N21	Root entry zone (lumbar spine), cauda equina	
N23	Conus medullaris (dorsal horn interneuron)	
P31	Brainstem (medial lemniscus)	
N34	Brainstem	
N37	Cortex (area 3b)	
P40	Cortex	
<b>C. Corresponding Components Between Median and Tibial Nerve SSEPs</b>		
<i>Median Nerve</i>	<i>Tibial Nerve</i>	<i>Origin</i>
N10	N8	Peripheral nerve (distal plexus)
N11 (P11)	N21	Proximal peripheral nerve
N13	N23	Spinal cord (dorsal horn interneuron)
P14	P31	Brainstem (medial lemniscus)
N18	N34	Brainstem
N20	N37	Cortex (area 3b, post central gyrus)
P26	P40	Cortex

Table 4-1A. (These are reasonable assumptions based on the currently available knowledge and may be subject to change depending on future research progress.)

### MEDIUM- AND LONG-LATENCY SSEPS FROM UPPER EXTREMITY STIMULATION

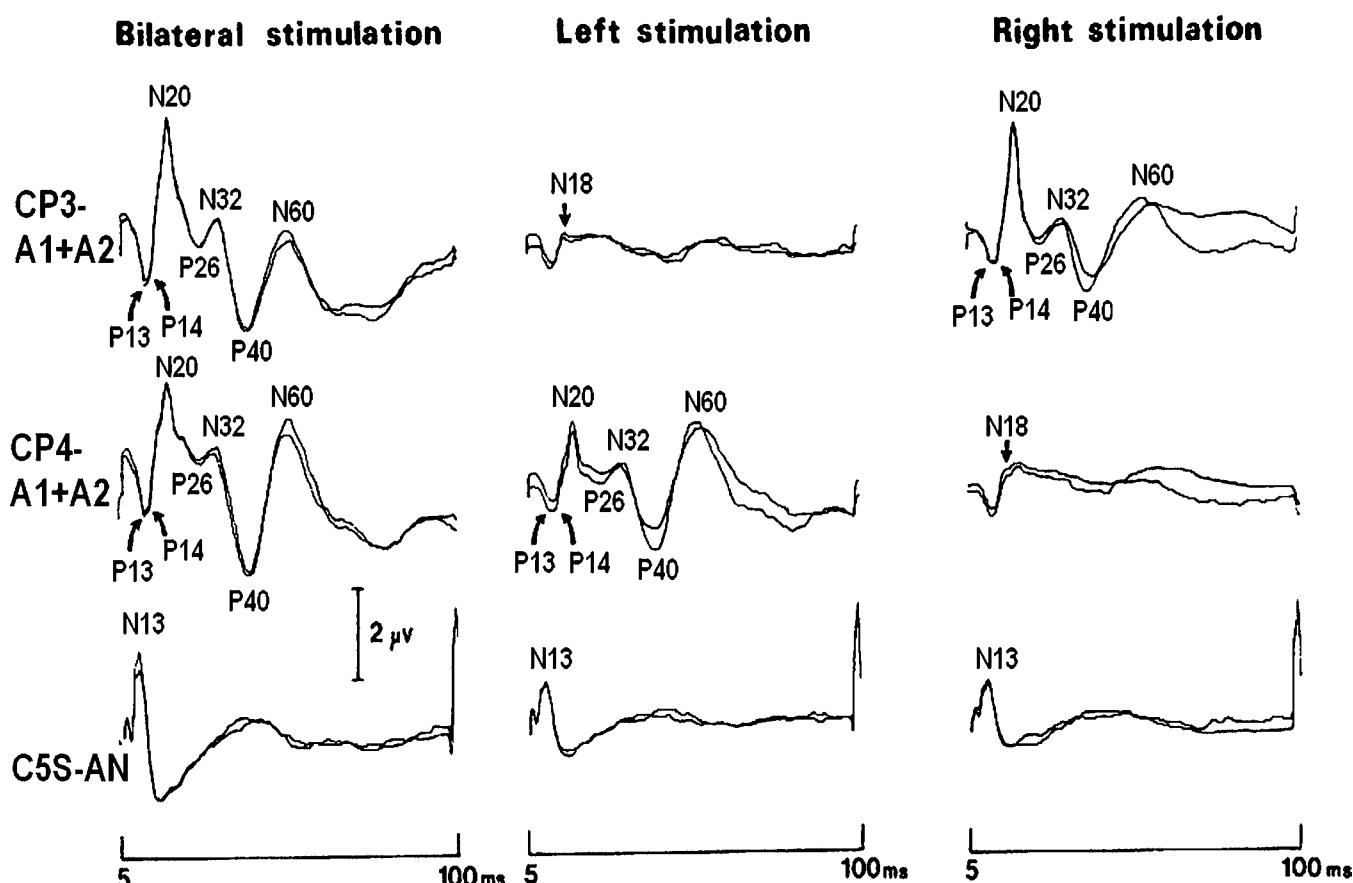
Following N20, a series of positive and negative waves follows. Those occurring after 30 ms but before 100 ms are generally considered medium-latency components. They are designated as P26, N32, P40, and N60 at the contralateral CP electrode (Fig. 4-15). Little is known about the physioanatomical substrates for P26 and N32 or subsequent peaks. It has been reported that various cognitive functions affect P40 and latter peaks.<sup>65,66</sup> Long-latency components are those occurring after 100 ms. Unlike short-latency components, medium- or long-latency components change depending on level of consciousness, vigilance, attention to or distraction from the stimulus, or other various cognitive functions. Components up to N60 are localized to the contralateral CP electrode (see Fig. 4-15), but subsequent peaks P100, N150, P250 and N350 are localized more closely to the

midline and these late peaks disappear with fast stimulus rates (Fig. 4-16).

In sleep, long-latency components (>100 ms) totally disappear and medium-latency components (N30, P40, and N60) sensitively change in amplitude and latency. As sleep deepens, N30, P40, and N60 show latency prolongation and amplitude diminution, with a greater degree in the later components (Fig. 4-17). Because of this variability, assessing medium- and long-latency components by comparing two separate trials obtained by the left- and right-sided stimulations is problematic and unreliable.<sup>66</sup> Most newer EP instruments, however, allow stimulating left and right sides alternately, so that the responses can be obtained within the same time domain and under the same conditions. Then, the responses by left- and right-side stimulations can reliably be compared.

### LOWER EXTREMITY SSEP

The most commonly used stimulation site for lower extremity SSEP is the tibial nerve at the ankle. The peroneal nerve at the popliteal fossa can also be used, but vigorous leg movements associated with the stimulus disturb the patient and the response



**Figure 4-15.** The relationship of SSEPs (including medium-latency components) between left/right unilateral stimulation and simultaneous bilateral stimulation in a normal subject. Note the symmetric responses between CP3 and CP4 by bilateral stimulation. The SSEP waveform from bilateral stimulation primarily consists of the contralateral response elicited by unilateral stimulation. Note N18 at the ipsilateral hemisphere in unilateral stimulation. (Modified from Yamada T, Dickins QS, Machida M, et al. Somatosensory evoked potentials to simultaneous bilateral median nerve stimulation in man: method and clinical application. In: Cracco RQ, Bodis-Wollner I, eds. *Frontiers of Clinical Neuroscience. Evoked Potentials*. Baltimore, MD: Williams & Wilkins, 1986:246–261, with permission.)

may be less consistent as compared to tibial nerve stimulation at the ankle. For pure sensory nerve stimulation, the sural nerve at the dorsum of the foot can be stimulated, but the spinal response may be less well defined compared to tibial nerve stimulation. In this chapter, SSEP following tibial nerve stimulation will be described.

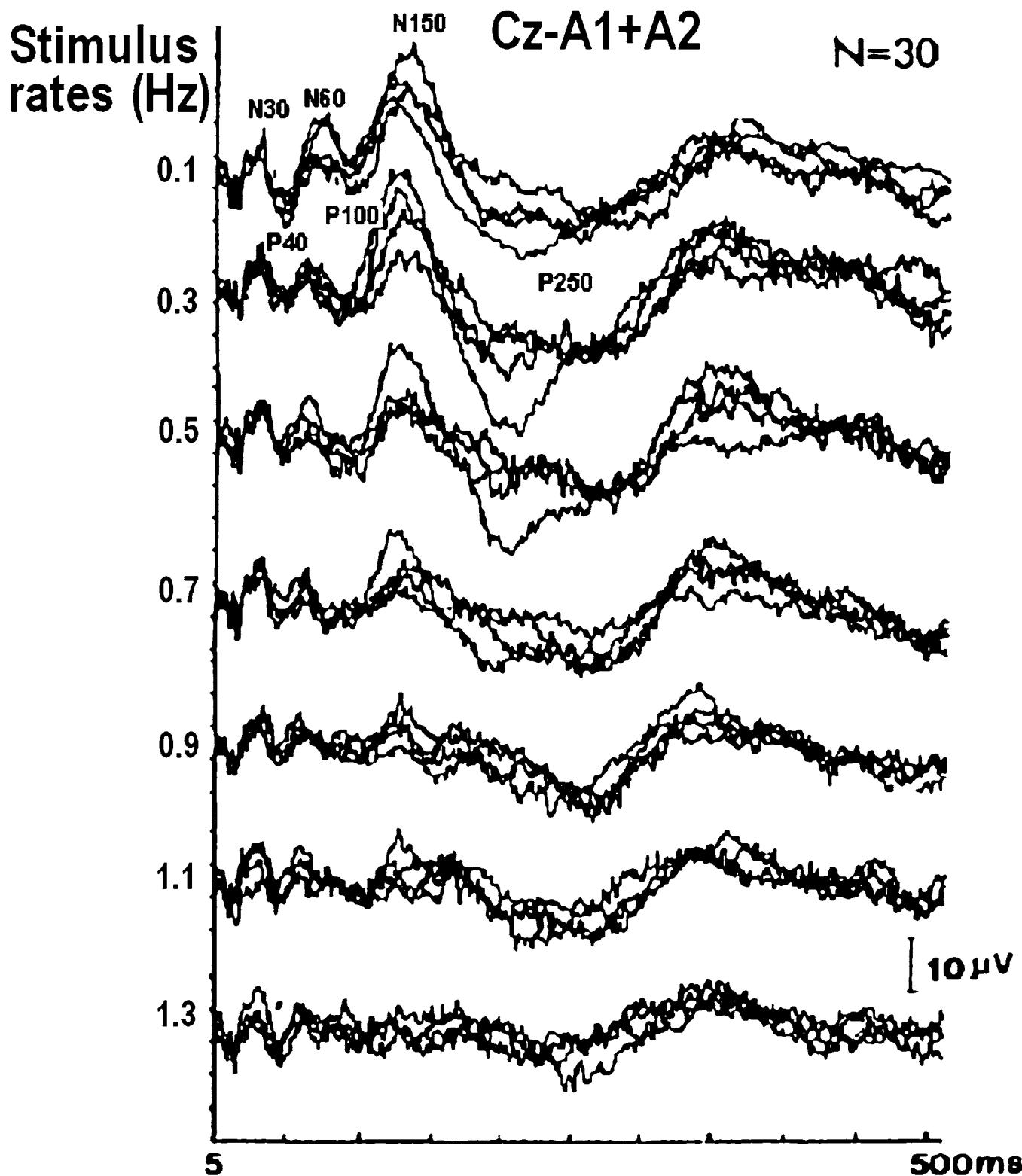
#### SPINAL RESPONSE

The spinal responses are best recorded from T12 spine (T12S) to L4 spine (L4S) (Fig. 4-18). A commonly used reference is the iliac crest. To locate the L4 spine, find a horizontal line connecting the left and right at the top of iliac crests. That line marks the level of L4 spine. T12S can be identified by finding the horizontal line connecting left and right last, floating rib (lowest rib), which corresponds to the T12 spine level.

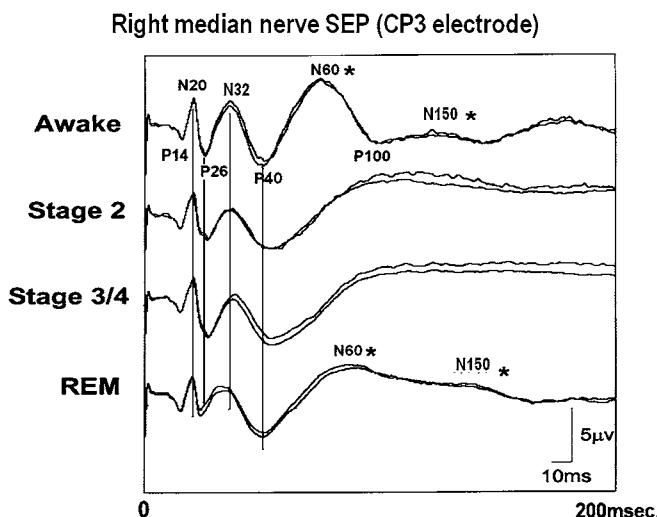
Similar to the cervical response in median nerve stimulation, the spinal response recorded from T12 or L4 consists of a triphasic (positive-negative-positive) peak and is distributed fairly widely from the lower thoracic to the upper lumbar spine. At T12S or L1S, the negative peak latency is about 23 ms (N23). The T12 or the L1 spinal potential often shows a small notched

wave over the rising phase of N23 (Fig. 4-19). This corresponds to the negative peak of L4 (N21). N21 is thought to arise from the cauda equina. N23 likely reflects postsynaptic activity at the conus medullaris.<sup>67,68</sup> Similar to the median nerve's N13 (cervical), which has a dipole positive field at the anterior neck, N23 yields a horizontally oriented dipole with positivity at the abdomen.<sup>69</sup> Because of this field distribution, T12/L1 spinal potential can be referenced to the abdomen, just like N13 (cervical) is referenced to the anterior neck. However, the most commonly used reference for N23 is the iliac crest because of the ease of placing the electrode.

Further rostral spinal recordings register traveling waves with a progressive latency shift from caudal to rostral spine, but the responses are much smaller than N23 or N21 (see Fig. 4-18). Because it usually requires more than 5,000 averaged responses to yield a reliably measurable response at the rostral spine, even in a cooperative and relaxed subject, it is not practical for routine clinical application. For routine clinical use, N23 at T12/L1 spine is usually measured. Unlike cervical N13, N23 is not considered to be an obligate potential and may not be recordable in some normal subjects, especially in older or obese individuals.

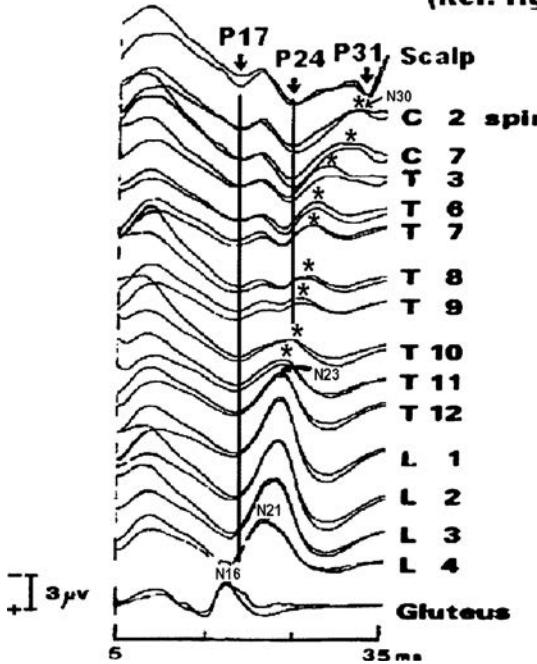


**Figure 4-16.** Effects of stimulus rate on long-latency SSEPs. Only 30 responses were summated for each response. The low filter setting was 1 Hz. Note the progressive decrease of late SSEP components, especially P100, N150, P250, and N350, with the increase of stimulus rate. N30-P40 components showed little change. (From Yamada T, Yeh M, Kimura J. Fundamental principles of somatosensory evoked potentials In: Lew HL, Kraft GH, eds. *Physical Medicine and Rehabilitation Clinics of North America*, vol. 15. Philadelphia, PA; Elsevier Saunders, 2004:19–42, with permission.)

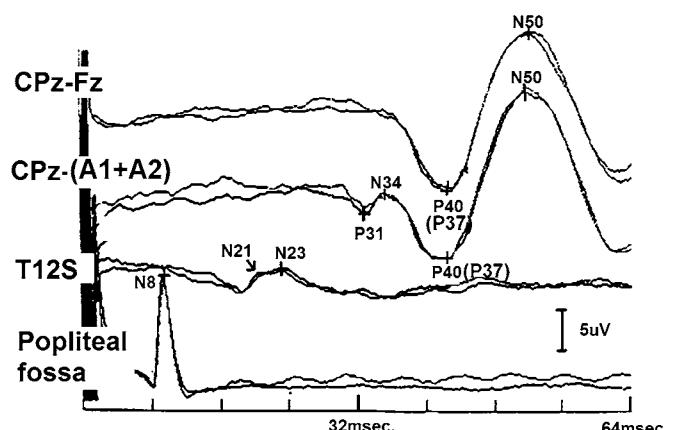


**Figure 4-17.** SSEP (including medium- and long-latency components) change in sleep. N60, P100, and N150 components sensitively disappear in non-REM sleep and recover somewhat in REM sleep. P26, N32, and P40 components remain but their latencies prolong in non-REM sleep and become close to the awake state in REM sleep. P14 and N20 remain unchanged [the detailed study of N20, however, has shown a slight prolongation in deep (stages 3 and 4) sleep].

### Left tibial Nerve Stimulation (Ref: right knee)



**Figure 4-18.** Scalp recorded FFPs and spinal potentials after stimulation of the tibial nerve. The spinal potentials are largest at T12 to L2 spine level and become smaller and longer in latency (shown by asterisks) when moving in a rostral direction. P17 FFP latency is close to N16 (nerve potential) recorded at the gluteus. P24 FFP latency is close to N23 (spinal potential) at T12 and L1 spine. P31 FFP latency is slightly longer than the negative peak of spinal potential recorded at C2S. The latency of L4 (spine potential N21) is shorter than N23 of T2-L1 spine potential. (From Yamada T, Machida M, Kimura J. Far-field somatosensory evoked potentials after stimulation of the tibial nerve. *Neurology* 1982;32:1151–1158, with permission.)

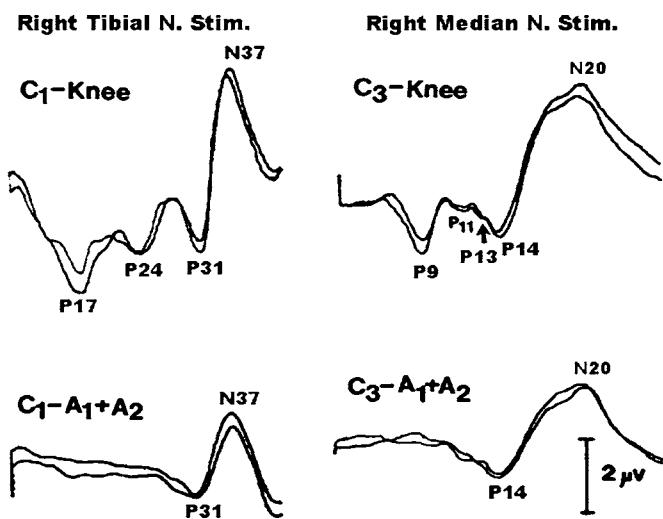


**Figure 4-19.** Four-channel tibial nerve SSEP. CPz-Fz records P40 (P37) and N50 but cancels out P31 FFP. Combined recording CPz with both Fz and ears (A1 + A2) reference helps to distinguish P31 and P40 (P37) by the presence of P31 only in CPz – (A1+A2), not in CPz-Fz derivation. T12S [with iliac crest (IC) reference] shows N23 (spinal cord potential), which often records a small notched wave (N21) over its rising phase. This is similar to the cervical spine recording in median nerve SSEP, which shows a notched N11 over the rising phase of the N13 potential. N21 and N23 likely correspond to N11 and N13 cervical potentials, respectively. N23-P31 IPL represents spinal cord conduction time and N23-P40 (P37) represents central conduction time that includes both spinal cord and brain conduction. (From Yamada T. Somatosensory evoked potentials In: Weinstein SL, ed. *The Pediatric Spine: Principles and Practice*. New York, NY: Raven Press, 1994:1171–1179, with permission.)

### SCALP POTENTIAL

When a scalp response is recorded with a noncephalic reference, it consists of three positive FFPs, that is, P17, P24, and P31 (see Fig. 4-18). This is comparable to median nerve FFPs, P9, P11, and P13/P14 (Fig. 4-20). Since P17 latency is close to the negative potential recorded at the low gluteus region (see Fig. 4-18), it likely originates from the distal portion of the sacral plexus and is equivalent to P9 of the median nerve SSEP.<sup>70,71</sup> Although P24 latency is close to N23 spinal potential, the origin of the scalp P24 is not established. Unfortunately, recording these FFPs using a noncephalic reference requires 5,000 or more averaged samples and has not been used for routine clinical application. Of these FFPs, P31 is the most easily recordable potential. P31 is equivalent to P14 of the median nerve SSEP and arises from the brainstem.<sup>70–72</sup> P31 can be recorded in most subjects with 1,000 to 2,000 summations using the ear or neck reference (see Fig. 4-20). P31 is a useful marker for measuring spinal cord conduction time by calculating the latency difference between N23 and P31 (see Fig. 4-19). Unlike P14 of median nerve, P31 is not an obligate potential and may not be recordable in some subjects. If P31 is not present, central conduction time is measured by the inter-peak latency of spinal N23 and cortical P40 (P37).

P31 is followed by N34 ipsilaterally and by N37 contralaterally (Fig. 4-21). N34 has a relatively widespread distribution and is recorded at bifrontal and ipsilateral central/parietal regions, which is similar to N18 of the median nerve SSEP. N34 is thus considered to be equivalent to N18<sup>72</sup> but may not be identifiable in some normal subjects. N37 is likely equivalent to N20 of median nerve SSEP, but this peak is also usually small and may not be present in some normal subjects. Therefore, clinical

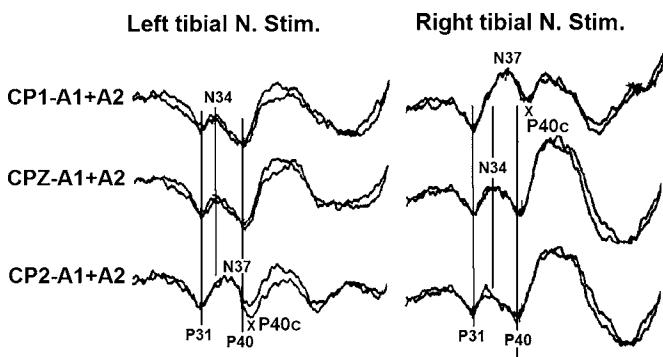


**Figure 4-20.** Comparison of tibial and median nerve SSEPs (contralateral responses) with distant (knee) reference and ear reference recording. Knee reference recordings show P17, P24, P31 FFPs in tibial nerve and P9, P11, P13/P14 FFPs in median nerve SSEPs. With ear reference, only P31 for tibial and P14 (P13/P14) for median nerve FFPs are recordable. P17 and P31 of tibial nerve SSEP correspond to P9 and P14 of median nerve SSEP, respectively. It is not certain if P24 of tibial nerve FFP is equivalent to P11 or P13 of median nerve FFP.

application of tibial nerve SSEP largely relies on the subsequent large positive potential, P40 (some refer it to as “P37”), which is usually largest at the midline or ipsilateral parietal electrode.

#### PARADOXICAL LATERALIZATION

Following N34, the subsequent positive peak, P40 (or P37) is best recorded at the midline (CPz) or ipsilateral hemisphere (CPi) (Figs. 4-22, see also Fig. 4-21). This is similar to the para-



**Figure 4-21.** Potential distribution of P31, N34, N37, and P40. P31 is equally distributed at ipsilateral, midline, and contralateral electrodes with ear reference recording. N34 is registered at midline and ipsilateral electrodes, and N37 is registered at contralateral electrode. The subsequent positive potential, P40, has larger amplitude and shorter latency at the midline and ipsilateral electrodes (paradoxical lateralization) than the positive potential (P40c) at the contralateral electrode (marked by x). (From Yamada T, Yeh M, Kimura J. Fundamental principles of somatosensory evoked potentials In: Lew HL, Kraft GH, eds. *Physical Medicine and Rehabilitation Clinics of North America*, vol. 15. Philadelphia, PA: Elsevier Saunders, 2004:19–42, with permission.)

doxical lateralization of P100 recorded in VEPs. Like cortical representation of visual inputs, cortical representation for the distal leg is situated in the mesial aspect of the hemisphere. The P40 (P37) field then projects to the ipsilateral hemisphere, creating ipsilaterally dominant field distribution over the scalp surface (see Fig. 4-22).<sup>73–75</sup> Subsequent peaks, N50 and P60, also show ipsilateral dominant distribution. Because of this paradoxical lateralization, P40 (P37) should be recorded at the midline (CPz) or 2 cm lateral (CP1 or CP2) to CPz, ipsilateral to the side of stimulation. The response from the contralateral hemisphere shows P31 and N37, and the following positive peak has a slightly longer latency than the ipsilateral P40 (P37) (see Fig. 4-21). Presumably, due to interindividual anatomical variations of cortical representation, P40 (P37) paradoxical lateralization is not a consistent finding in all subjects.<sup>76</sup> P40 (P37) may be maximum at CPz in some subjects. In a small number of normal subjects, it could be lateralized to the contralateral (CPc) hemisphere.

Paradoxical lateralization is applied only to distal leg stimulation such as tibial nerve at the ankle or sural nerve at the foot, but not for proximal leg stimulation such as lateral femoral cutaneous nerve stimulated at the inguinal ligament. Because the sensory cortex from the lateral femoral cutaneous nerve lies on the more lateral surface rather than the medial cortex, P40 (P37) appears on the contralateral hemisphere as shown in Figure 4-22, similar to the SSEP of the upper extremity.

#### RECORDING MONTAGES FOR LOWER EXTREMITY NERVE

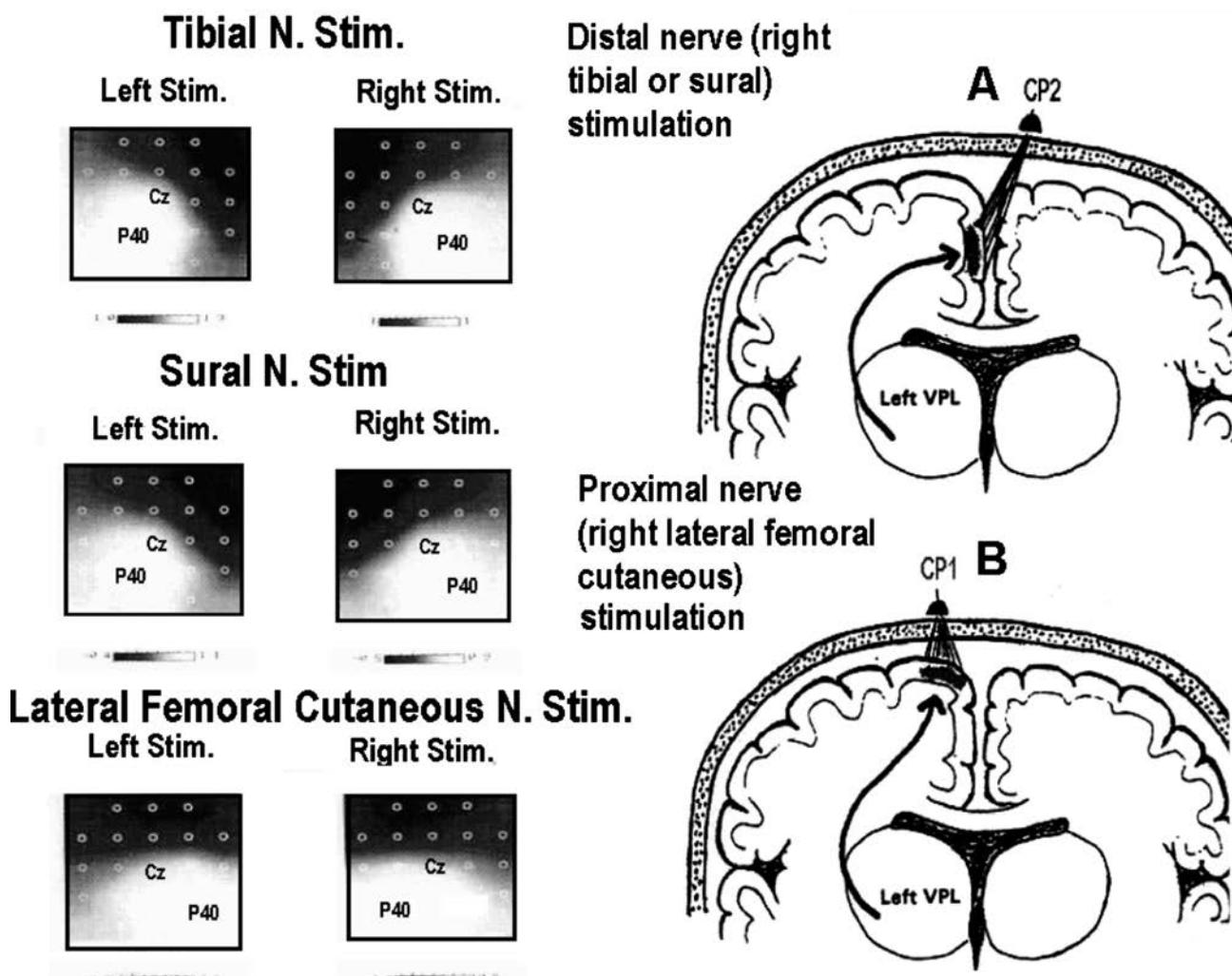
The ACNS recommends the following montage<sup>54</sup> (Fig. 4-23A)

- Channel 1: CPi-Fpz (P40)
- Channel 2: CPz-Fpz (P40)
- Channel 3: Fpz-C2S (P31, N34)
- Channel 4: T12S-Iliac crest (N23)

CPz is between the Cz and Pz electrodes and CPi is CP1 or CP2 (according to the modified combinatorial nomenclature by ACNS) and located between CPz and CP3 or CP4, respectively, ipsilateral to the side of stimulation. T12S can be identified by finding the horizontal line connecting left and right last, floating rib which corresponds to the T12 spine level.

#### Rationale for the Above Montage

Both CPz-Fpz and CPi-Fpz record NFP of P40 (P37). Both derivations cancel out FFPs of P31 (equivalent to P14 in median nerve SSEP) and N34 (equivalent to N18 in median nerve SSEP) FFPs. Fpz-C2S registers P31 and N34 FFPs. It should be noted that C2S electrode serves as a reference with little contribution from the cervical electrode itself. T12S records the N23 (lumbar) spinal potential that is equivalent to N13 (cervical) of upper extremity SSEP. P40 (P37) usually appears at both channels 1 and 2, and could be of greater amplitude either at CPz or CPi. In some subjects, however, either CPz or CPi may have a longer latency positive potential. In this case, the shorter latency potential is the “true” P40 (P37), and the longer latency potential is the contralateral response. These differences occur due to interindividual anatomical variations in cortical representation of the leg in relationship with the location of scalp electrodes.



**Figure 4-22.** Paradoxical lateralization can be applied only to distal nerve (tibial and sural nerves) stimulation, not to the proximal nerve (lateral femoral cutaneous nerve) stimulation. In both tibial and sural nerve stimulation, topographic mapping showed P40 distribution (*positivity is shown in white*) was skewed to the ipsilateral hemisphere, that is, left hemisphere dominant P40 to left side stimulation and vice versa. In contrast, the lateral femoral cutaneous nerve produced a P40 distribution more on the contralateral hemisphere. This can be explained by the anatomical representation of the distal nerve that is situated in the medial aspect of the hemisphere. Activity from the medial aspect projects more to the electrode on the contralateral side that is ipsilateral to the side of stimulation (A). In contrast, cortical representation of the proximal nerve is situated more on the lateral surface of the hemisphere; thus, the activity is picked up on the same hemisphere, i.e., contralateral to the side of stimulation (B), which is similar to the upper extremity SSEPs. (From Yamada T. Neuro-anatomic substrates of lower extremity somatosensory evoked potentials. *J Clin Neurophysiol* 2000;17:269–279, with permission.)

An alternative montage follows (Fig. 4-23B).

Channel 1: CPi-A1+A2 (P31, N34, P40)

Channel 2: CPz-Fpz (P40)

Channel 3: T12S-Iliac crest (N23)

Channel 4: Popliteal fossa-knee cap (N8)

The popliteal fossa electrode is to record the nerve action potential with the active electrode placed on the skin overlying the nerve at the popliteal fossa and the reference electrode several centimeters away, for example, on the knee cap.

#### Rationale for the Above Montage

Channel 1 records P31 and N34 FFPs and P40 (P37) (cortical potential). Channel 2 records P40 (P37) cortical potential only. Channel 3 registers N23 spinal potential and channel 4 records the peripheral nerve potential (N8) at the

popliteal fossa. Channels 1 and 2 register P40 (P37), but P31 appears only in channel 1. This helps to distinguish P31 and P40 (P37). Channel 4 monitors the integrity of the peripheral nerve input. The absence of this popliteal potential indicates peripheral nerve problem (peripheral neuropathy), improper electrode placement, or inadequate stimulus delivery.

Another alternative montage is (Fig. 4-24)

Channel 1: CPz-Fpz (P40)

Channel 2: CPi-A1+A2 (P31, N34, P40)

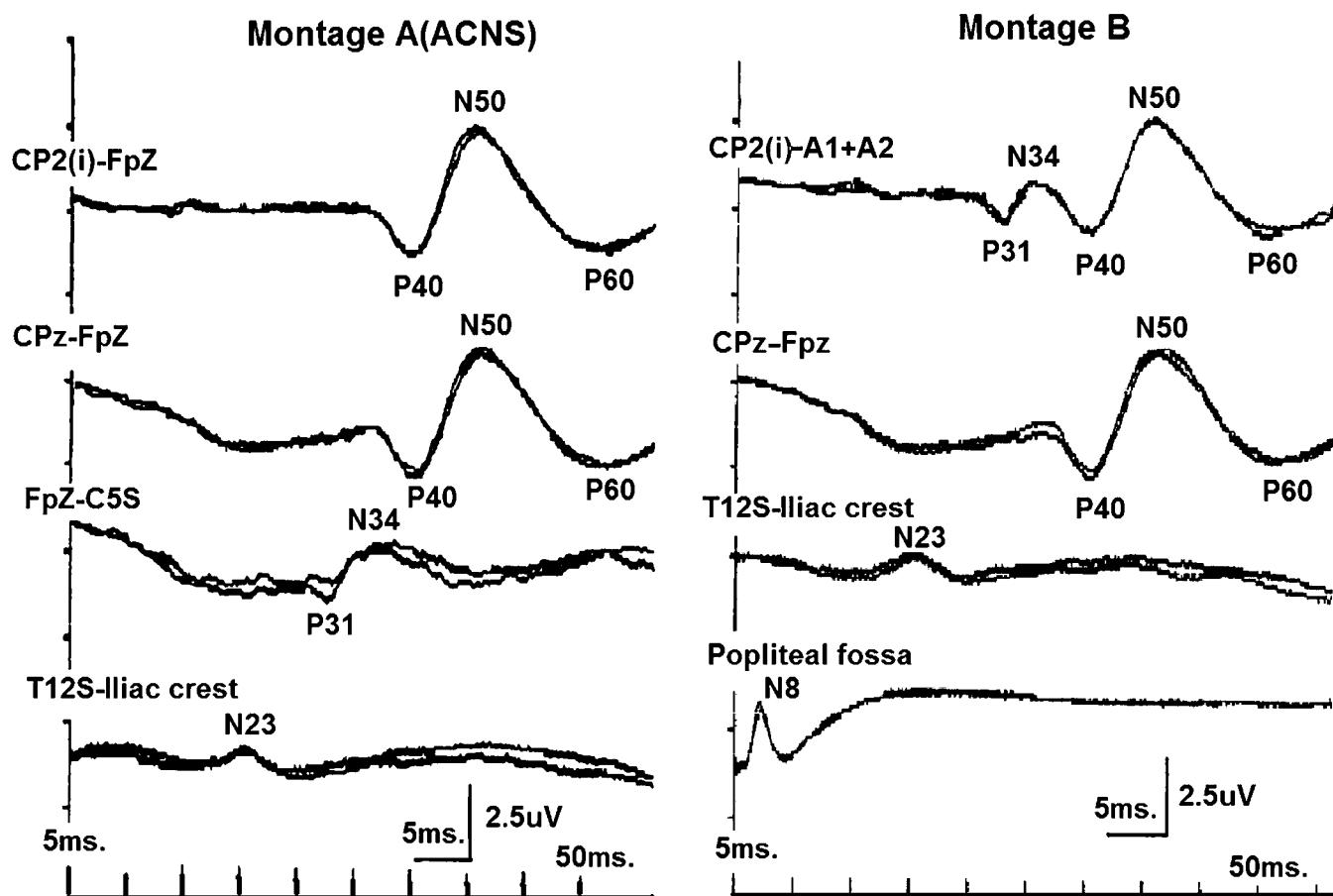
Channel 3: CPz-A1+A2 (P31, N34, P40)

Channel 4: CPc-A1+A2 (P31, N37, P40)

Channel 5: T12-iliac crest (N23)

Channel 6: Popliteal fossa reference (N8)

## Right tibial N. stimulation



**Figure 4-23.** Comparison of two montages for lower extremity SSEP. Montage A (recommended by the ACNS) uses two scalp electrodes from ipsilateral and midline electrodes, both referenced to Fpz. Both register P40 (P37). The 3rd channel is a far-field recording registering P31 and N34 FFPs arising primarily from Fpz electrode (it should be noted that C5S is the reference electrode and has practically no potential from this electrode). The 4th channel records the spinal potential of N23. Montage B uses different references for scalp recording. The ear reference recording registers both P31 and N34 FFP and P40 (P37) cortical response, while the Fpz reference records only the cortical potentials (canceling FFPs). This montage allows for monitoring the peripheral potential at the popliteal fossa, yielding N8.

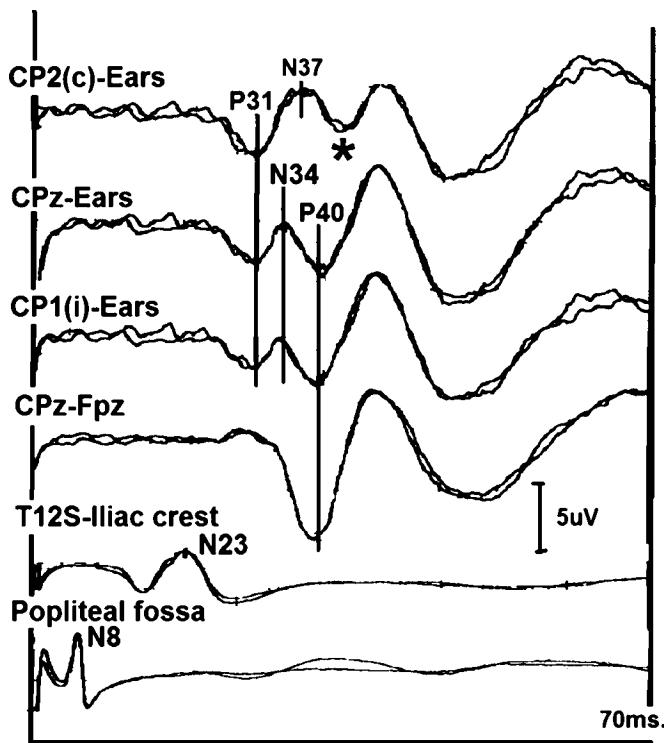
### Rationale for the Above Montage

Recording ipsilateral, midline, and contralateral responses aids in correctly identifying paradoxically lateralized P40 (P37). P40 (P37) usually appears at CPz and CPi electrodes and a slightly delayed positive potential appears at CPc (P40c). Due to anatomical variations, however, in some subjects, P40 (P37) may have the shorter latency at CPc than at CPi or CPz electrode. In this case, the shorter P40 (P37) should be measured as P40 (P37) potential. The combination of channels 1 through 4 also helps to distinguish P31 and P40. At the spine, an additional recording may be placed at L4 spine that records a slightly shorter latency negative spinal potential (N21) than N23 at T12 spine. N21 represents the cauda equina potential, which may be equivalent to N11 recorded at the cervical spine in upper extremity SSEP.

Table 4-1B shows main tibial nerve SSEP components in relationship with anatomical origins, and Table 4-1C lists corresponding components between tibial and median nerve SSEP.

### ABNORMAL CRITERIA

Normative data should be obtained from a population including various arm lengths or heights. After the age of 3 to 5 years, the absolute latencies of short-latency SSEP are linearly correlated with the arm length for upper extremity SSEP and with the height or leg length for lower extremity SSEP (see Appendix Figs. 4A-1 to 4A-12). Leg length or height can be ignored in assessment of interpeak latencies (IPLs), or on the differences of absolute as well as IPLs between left- and right-sided stimulations. The upper limit of normal is usually 2.5 or 3 standard deviations above the mean. The amplitude criteria cannot be established with Student-t test because of considerable individual variability and non-Gaussian distribution in the normal population. The most reliable amplitude abnormality is the absence of obligate potentials. On the other hand, some consider the amplitude depression greater than half of one side compared to the other side abnormal, assuming that the stimulation intensities are comparable between the two sides.



**Figure 4-24.** Alternative montage with a greater number of channels. Because of anatomical variations, paradoxical lateralization is not a consistent finding. Extra channels including all three CP sites (ipsilateral, contralateral, and midline electrodes) help to identify P40 correctly.

## OBLIGATE POTENTIALS

### Upper extremity SSEP, Lower extremity SSEP

Erb's potential, N10 (U); Popliteal potential (L)

Cervical potential, N13 (U); Cortical potential, P40 (P37) (L)

Scalp recorded, P13/P14 (U)

Scalp recorded, N18 (U)

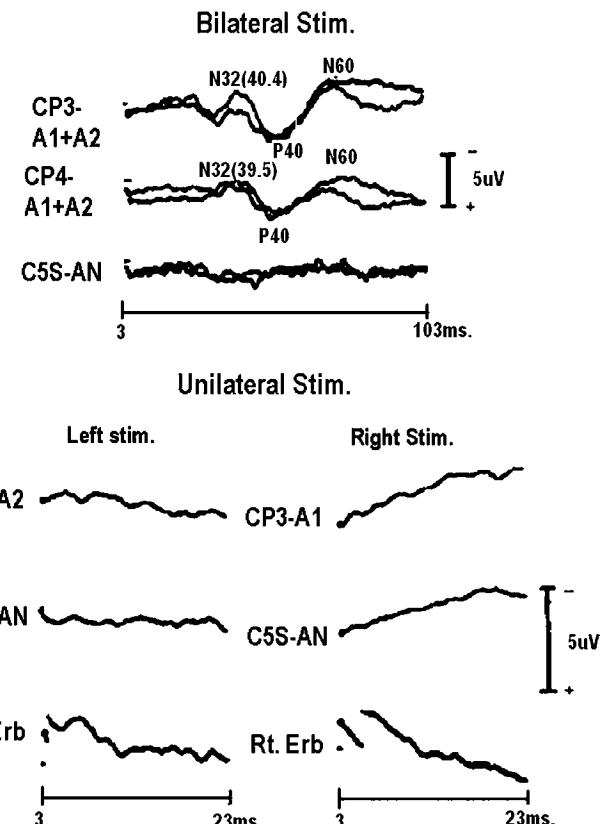
First cortical potential, N20 (U)

*The popliteal potential is an obligate potential unless the patient has peripheral neuropathy. Recording of popliteal potential is important to evaluate the adequacy of stimulus delivery. Although N13 cervical and P14 scalp potentials of upper extremity SSEP are obligate potentials, the corresponding N23 spinal and P31 scalp potentials of lower extremity SSEP are not. (U) for upper and (L) for lower extremity.*

## ANATOMICAL CORRELATES OF SSEP ABNORMALITIES

### PERIPHERAL NERVE LESIONS

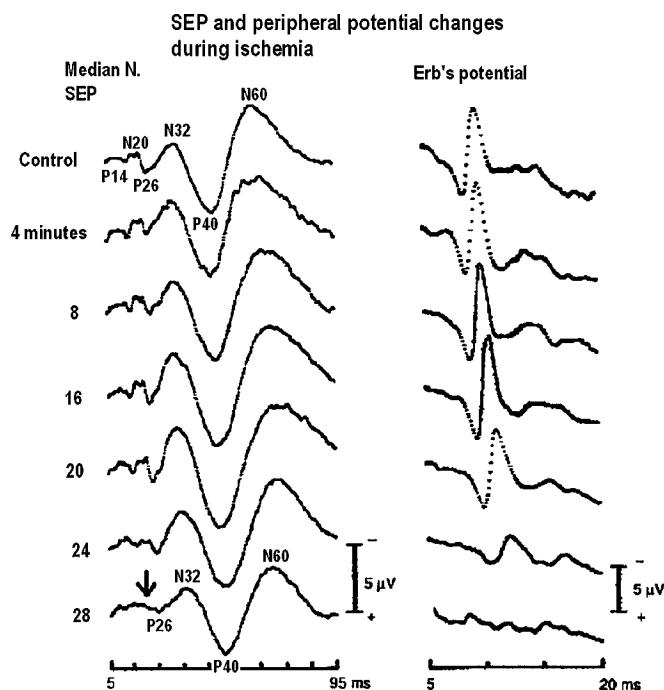
With a mild degree of peripheral neuropathy, SSEP is normal or may show a mild prolongation of all components including Erb's potential. In order to correctly diagnose this condition, normal data that correlate with the arm length for median and the height for tibial nerve SSEPs are required (see Appendix Figs. 4A-1 to 4A-12). If a peripheral problem is



**Figure 4-25.** An example of abnormal median nerve SSEP secondary to peripheral neuropathy. Note there was no short-latency SSEP including Erb's potential, N13 (cervical response), and N20 (cortical response), but medium-latency potentials (N32, P40, N60) were present with bilateral stimulation. (From Yamada T, Kimura J, Wilkinson T, et al. Short- and long-latency median somatosensory evoked potentials. Findings in patients with localized neurological lesions. *Arch Neurol* 1983;40:215–220, with permission.)

suspected, a detailed nerve conduction study should be performed. When peripheral neuropathy is severe to the extent that Erb's potential is absent, scalp SSEP, especially medium-latency components after N20 (N30-P40-N60), may still be recordable (Fig. 4-25). This is demonstrated in our experimental study in which Erb's potential was abolished by tourniquet-induced ischemia but the scalp SSEP, especially the later peaks, was still recordable even with an absent N20 (Fig. 4-26). It was postulated that the later components remained due to the still-functioning smaller and slower-conducting fibers despite a failed conduction of the larger and faster-conducting fibers as long as the patient feels the stimulus delivery.<sup>77</sup> An alternative explanation is that the desynchronized inputs at the peripheral nerve are still sufficiently synchronized at the central level (central amplification factor) producing the medium latency SSEP.<sup>78</sup>

When the peripheral nerve is affected proximally, for example in a *brachial plexus injury* or *thoracic outlet syndrome*, SSEP may or may not be abnormal, depending on the severity and extent of the lesion. It should be noted that the Erb's potential is generated by the ascending volley of sensory and antidromic



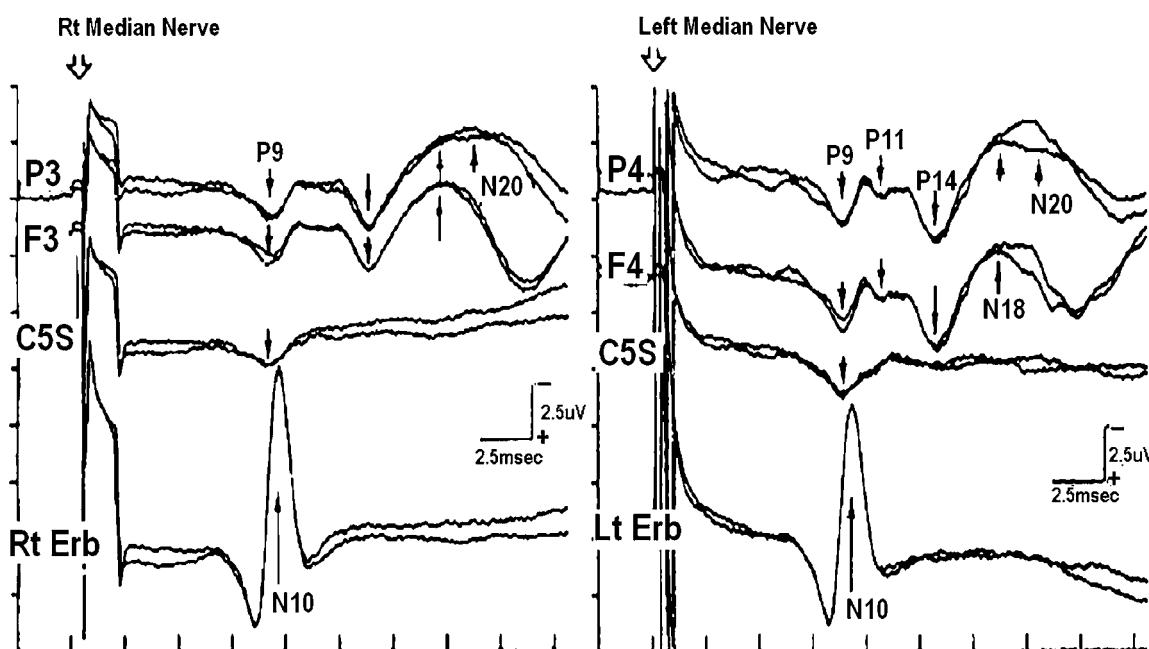
**Figure 4-26.** The relationship of SSEP and Erb's potential changes by making the arm ischemic by inflated blood pressure cuff in a normal subject. There were both progressive latency prolongation and amplitude decline of Erb's potential as the time of ischemia progressed. At 28 minutes of ischemia, there was no Erb's potential but robust medium-latency potentials (N32, P40, N60) were still present despite the absence of N20 (shown by arrows) (From Yamada T, Muroga T, Kimura J. Tourniquet-induced ischemia and somatosensory evoked potentials. *Neurology* 1981;31:1524–1529, with permission.)

volley of motor filters when the median nerve is stimulated at the wrist. Also, the median nerve is derived from multiple segments of nerve roots from C6, C7, C8, T1, and a part of C5. If the lesion affects only one or a few segments of nerve root or only motor fibers, Erb's potential and other SSEP components remain intact. When dorsal root ganglia are affected at multiple segments, Wallerian degeneration takes place within 5 to 10 days after injury and Erb's potential, as well as the nerve action potentials at further distal sites, will be lost.

In the lower extremity nerves, peripheral nerve lesions cause a delayed popliteal potential (PP) and/or prolongation of the PP-N23 IPL. The assessment of these latencies must be based on normal data that are correlated with height or leg length (see Appendix Figs. 4A-8 to 4A-12). Because the N23 (spinal potential) may not be present in some normal subjects, it is often not possible to differentiate peripheral versus central lesions when N23 is not recordable.

#### CERVICAL CORD/ SPINAL CORD LESIONS

The evaluation of a cervical lesion focuses on N11 and N13. Dissociated findings with normal N11 and absent N13 have been reported in lower cervical cord lesions.<sup>79</sup> The origin of N11 has been debated, but it is thought to arise from the dorsal column<sup>80</sup> or the root entry zone (proximal to the dorsal root ganglion).<sup>37,41</sup> A large cervical cord lesion affecting the root entry zone has been shown as an abnormal N11.<sup>38</sup> A clear prolongation of the N11–N13 IPL indicates a cervical cord lesion, likely at the lower cervical cord. However, since N11 is not an obligate potential, it is often difficult to decide if N11 is intact or affected.

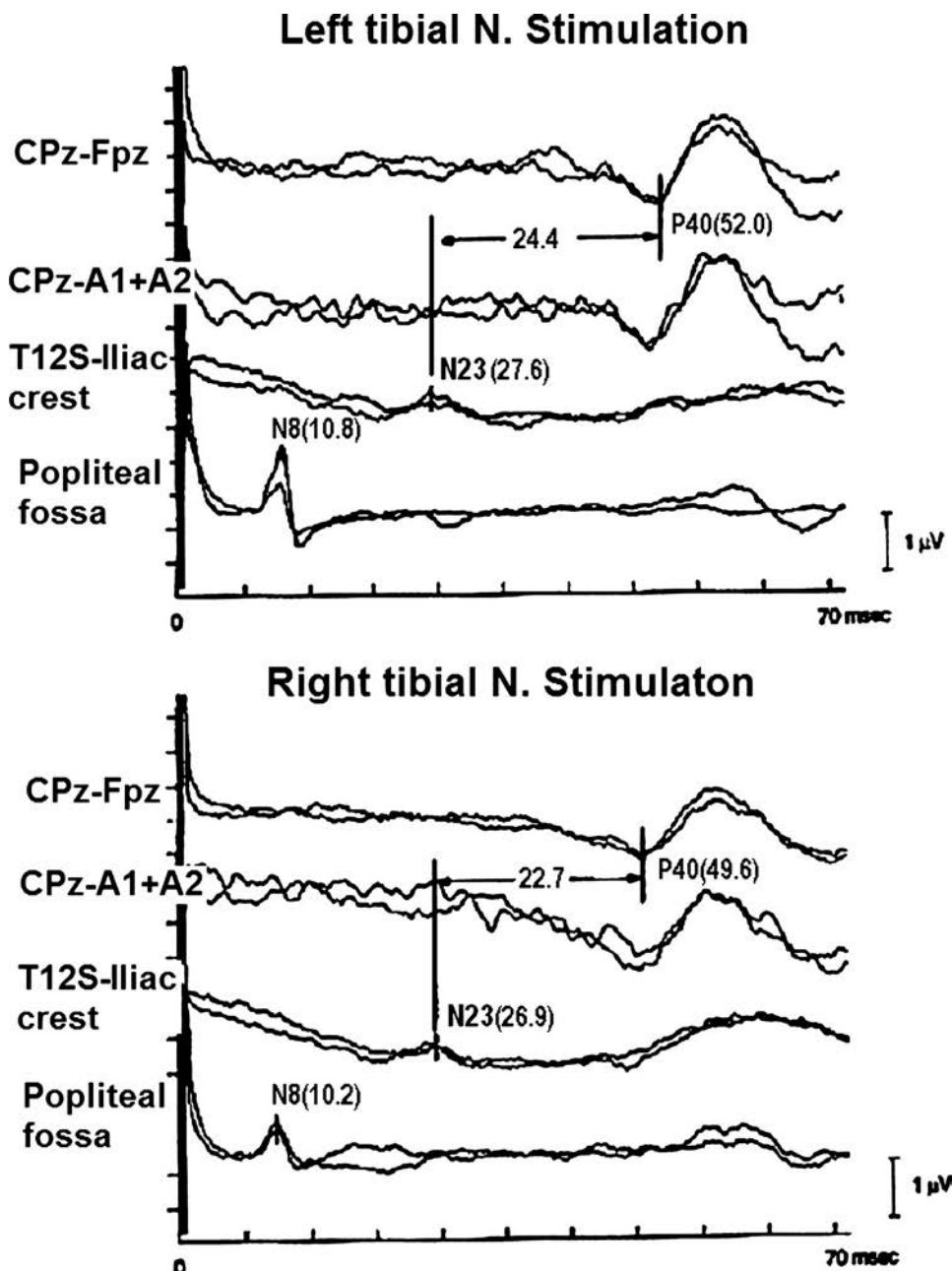


**Figure 4-27.** An example of cervical cord lesion in a patient with syringomyelia. Note the absence of N13 (cervical) in association with normal P14, N18, and N20 (reference = contralateral Erb's point). This supports the notion that N13 (cervical) is generated by dorsal horn interneurons at the central spinal cord and is independent from the dorsal column-medial lemniscus system. (From Urasaki E, Wada S, Kadoya C, et al. Absence of spinal N13-P13 and normal scalp far-field P14 in a patient with syringomyelia. *Electroencephalogr Clin Neurophysiol* 1988;71:400–404, with permission.)

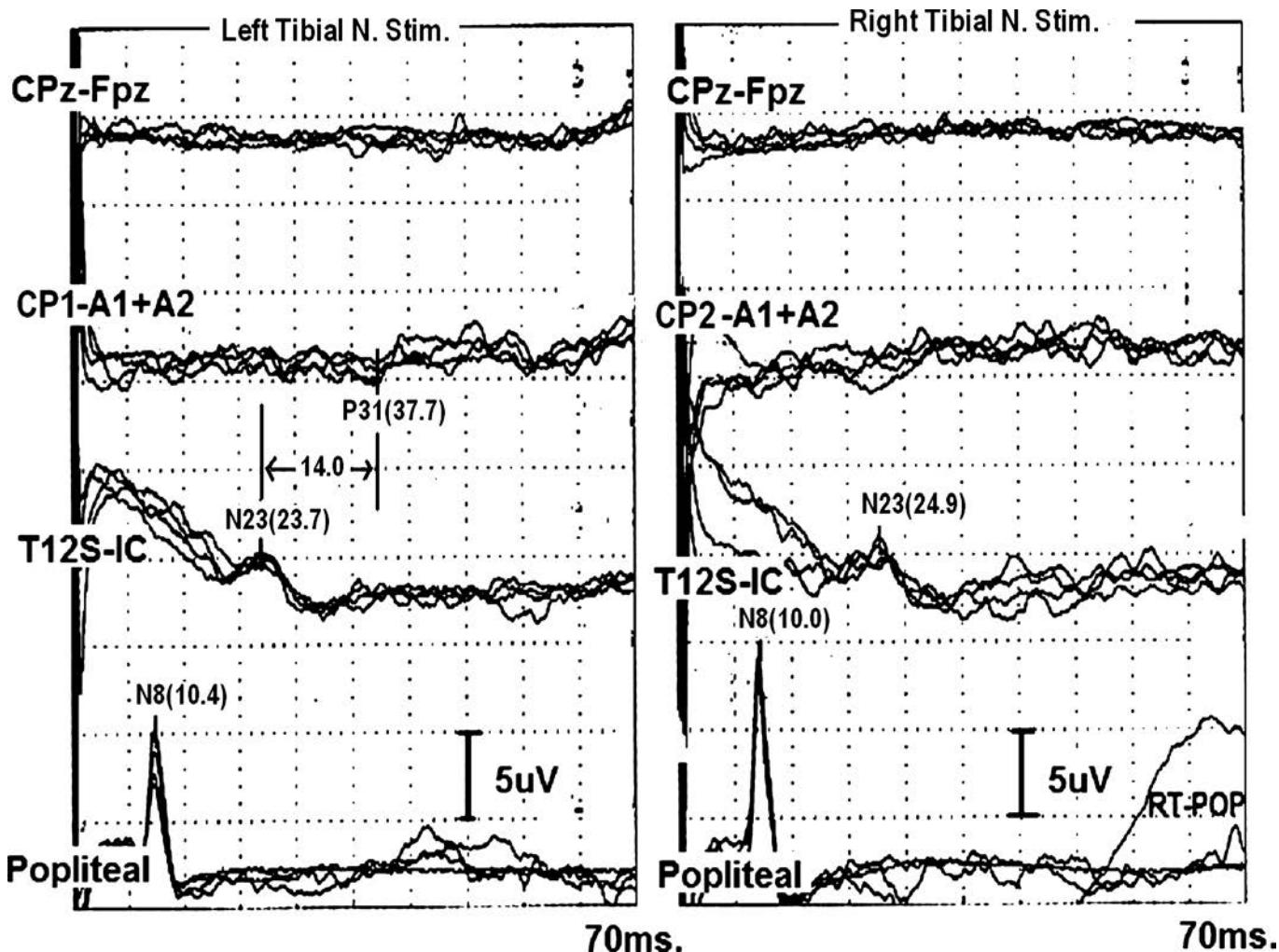
It is agreed that N13 (cervical potential) arises from the dorsal horn interneurons (central gray matter).<sup>59,60</sup> An abnormal N13 in patients with syringomyelia<sup>61,62</sup> is consistent with this view (Fig. 4-27). These patients may show a normal P14, N18, and N20 scalp recorded potentials, supporting the concept that N13 is independent from the dorsal column-medial lemniscus pathway.

In lower extremity SSEP, scalp recordings may be abnormal with a cervical cord lesion showing either a prolonged P31 or P40 (P37) with a normal N23 (spinal) resulting in a prolonged

central conduction time (Fig. 4-28) or an absent scalp potential (Fig. 4-29). But this abnormality does not allow differentiation between thoracic or lumbar cord lesions because it is not possible to record a cervical potential or a traveling impulse of the spinal cord after tibial nerve stimulation unless an extremely large number of repetitions are performed (see Fig. 4-18). If N23 at the T12 (or L1) spinal level is normal, it is reasonable to conclude that the lesion is at least above the conus medullaris (see Figs. 4-28 and 4-29).



**Figure 4-28.** An example of abnormal tibial nerve SSEP in a patient with spinal cord tumor. Note the prolonged N23-P40 IPL (upper limit of normal is 21.5 ms). Although N23 latency is longer than the mean latency, it is normal for this patient as his height is 180 cm (see Fig. 4A-9). Because there is no P31 (subcortical potential), it is not possible to differentiate spinal cord versus brain/brainstem lesion.



**Figure 4-29.** An example of abnormal tibial nerve SSEP in a patient with spinal cord injury. The N8 (popliteal potential) and the N23 (spinal potential) were normal. No cortical or subcortical potentials were present to right stimulation, but possible P31 (subcortical potential) might be present to left-side stimulation. If so, N23-P31 IPL was abnormally prolonged (upper limit of normal is 11.0 ms), indicating a lesion within the spinal cord. (The numbers in parentheses indicate latency values in ms.)

#### HIGH CERVICAL CORD AND BRAINSTEM LESIONS

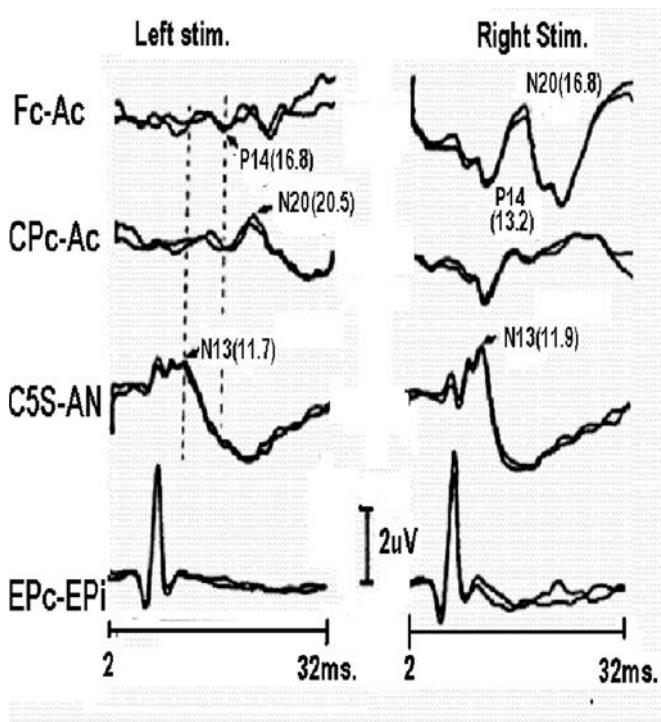
Scalp recorded P14 FFP arises from the medial lemniscus.<sup>43,81,82</sup> A lesion at the high cervical cord,<sup>43</sup> medulla,<sup>53</sup> or cervicomedullary junction<sup>80</sup> shows either an absent or a prolonged P14 with an associated normal N13 (cervical) (Figs. 4-30 and 4-31). N13 at the high (C2S) and low (C5S) cervical spine have been proposed to arise from separate generators.<sup>55,56</sup> If so, a high cervical cord lesion could selectively affect C2S-N13, leaving C5S-N13 intact.

Although P13 and P14 were regarded as a complex arising from the same generator (medial lemniscus), it is most likely that they arise from separate generators. It has been proposed that P13 reflects the postsynaptic activity of the cuneate nucleus and P14 reflects the medial lemniscus volley by finding the dissociated alteration of P13 and P14 in clinical cases.<sup>74,83,84</sup>

#### THALAMIC LESIONS

Because P14 is of brainstem origin, a lesion involving the thalamus is expected to affect the SSEP components after P14. The subsequent negative peak after P14 is N18, which is a widespread potential, most prominently at the bifrontal electrodes. Earlier studies thought N18 to be of thalamic origin.<sup>45,46</sup> Later studies, however, found that N18 was normal in a patient with a pontomedullary junction lesion<sup>48</sup> but affected in patients with midbrain-pontine lesions.<sup>85-87</sup> Furthermore, N18 latency matches the negative activity recorded directly from the pontine area.<sup>84</sup> These studies imply that N18 arises from the midbrain—pons area. A patient with a small thalamic lesion affecting the VPL nucleus showed a normal P14 and N18 but absent N20 (Fig. 4-32), which also supports this view.

Because all sensory pathways converge at the VPL nuclei, even a small lesion there would result in a severe sensory deficit



**Figure 4-30.** An example of median nerve SSEP in a patient with high cervical cord lesion. Note prolonged P14 and prolonged N13-P14 IPL (shown by dotted line; upper limit of normal is 2.4 ms) with depressed and prolonged N20 after left-sided stimulation. The SSEP to right-side stimulation was normal.

to all modalities of sensation associated with total absence of SSEP components after N18. A thalamic lesion not affecting the VPL nuclei is likely to show a normal short-latency SSEP but may affect later components.<sup>88,89</sup>

#### CORTICAL/HEMISPHERIC LESIONS

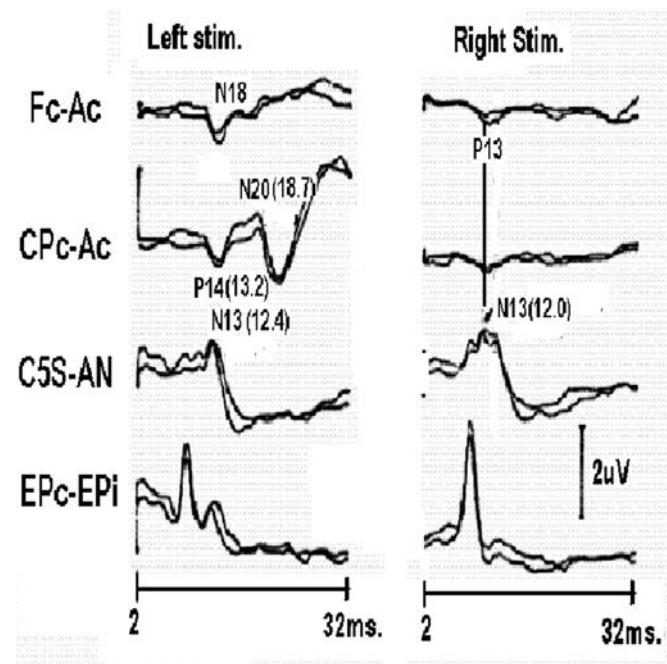
The first cortical potential, N20, is assumed to be generated at area 3b (primary sensory cortex) of the postcentral gyrus. A cortical lesion affecting the primary sensory cortex, therefore, shows either a delayed (Fig. 4-33) or an absent N20 (Fig. 4-34). A N20 recorded with a noncephalic or ear reference normally includes both N18 and N20 components. Therefore, if N20 is absent, the CPc electrode shows N18 only due to a deprived N20 (see Fig. 4-34, see also Fig. 4-37).

If a lesion in the cerebral hemisphere does not directly affect the primary sensory pathway, N20 is normal but the later potentials (N30, P40, N60) may be affected (Figs. 4-35 and 4-36).

#### SSEP IN SPECIFIC NEUROLOGIC CONDITIONS

##### MULTIPLE SCLEROSIS (MS)

As with other evoked potential studies, MS is the most commonly encountered clinical condition where SSEP studies are requested. The usefulness of SSEPs in MS is based on their ability to detect clinically “silent” focal lesions affecting the sensory



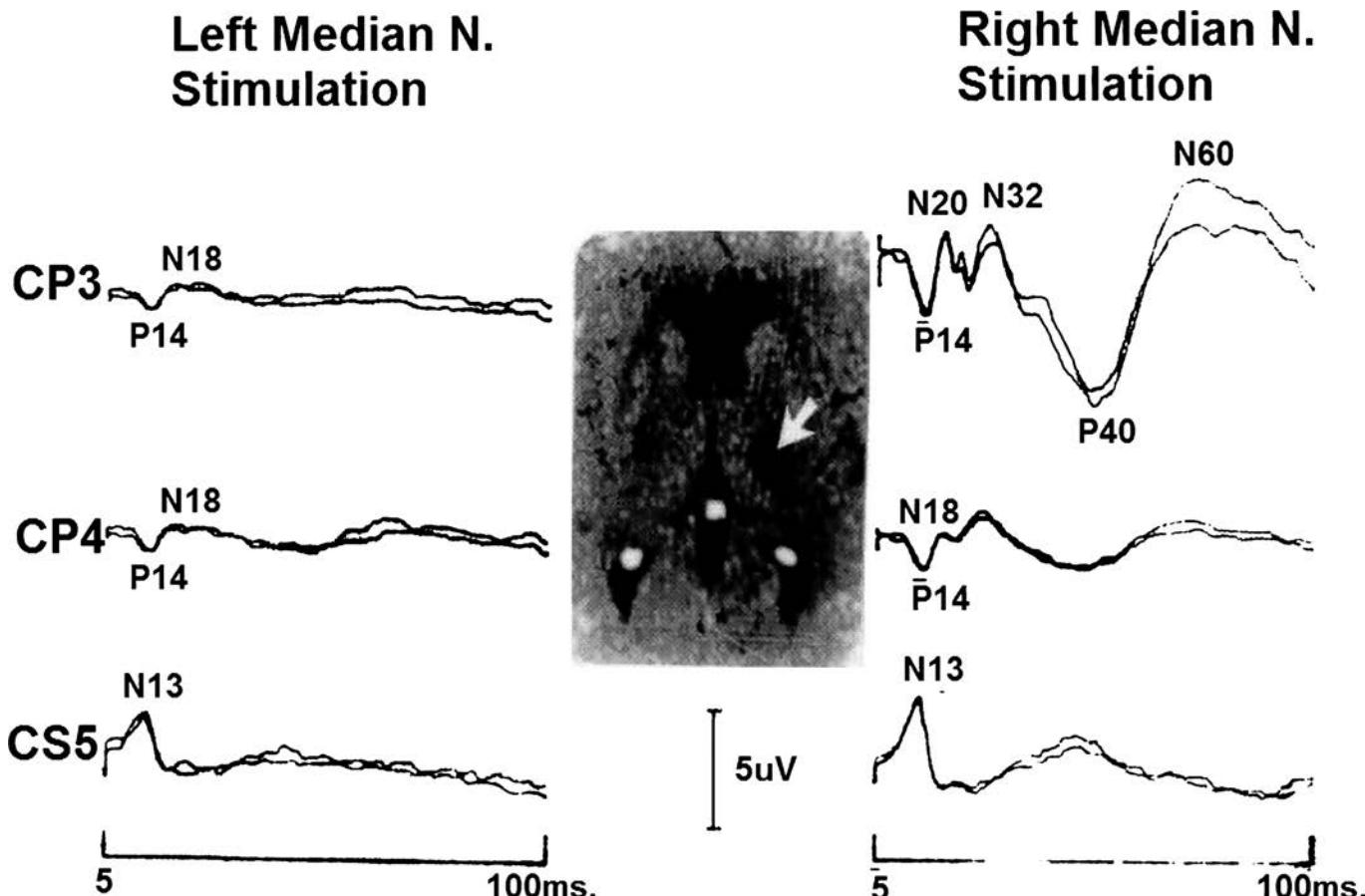
**Figure 4-31.** An example of abnormal SSEP in a patient with a brainstem lesion. Left-sided stimulation was normal. Right-side stimulation shows no scalp response within 32 msec after the stimulus except for a small dip that was likely P13 associated with normal N13 (cervical). This indicated the absence of P14 and N20.

pathways. Abnormal SSEPs without clinical evidence of sensory deficit or with abnormality of another modality of evoked potentials raise a strong possibility of MS diagnosis. Latency prolongation associated with well-preserved amplitude and/or wave form is characteristic of a demyelinating process.

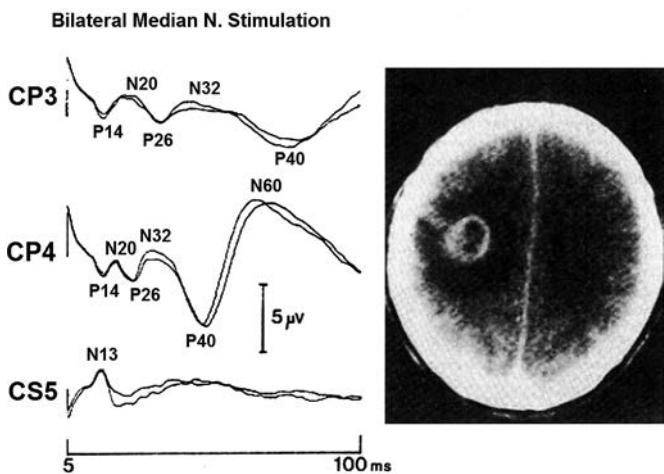
A large number of SSEP studies in patients with MS are available.<sup>90-98</sup> Most agree that the incidence of abnormal SSEP in patients with definite MS group is close to 80%, the probable group 60%, and the possible group 40% for median nerve SSEP. Slightly higher incidences of abnormalities were noted in lower extremity SSEP in each group of MS patients. This is likely due to a longer tract of the sensory pathway in the lower than in the upper extremity SSEP. In definite MS patients, about 90% had an abnormal SSEP either in upper or lower extremities. Of these, about 60% had abnormalities in both upper and lower extremity SSEPs.<sup>97</sup> When all groups of MS patients are combined, about 60% (upper extremity) and 70% (lower extremity) of MS patients have abnormal SSEPs.

Diverse types of SSEP abnormalities have been found including absence or prolongation of N13 (cervical potential), prolongation of N13-P14 IPL (cervical cord to brain stem conduction time), prolongation of N13-N20 (central conduction time), and abnormal N20 associated with normal preceding subcortical potentials. In some MS patients, the abnormality may be limited to the medium-latency components (N30-P40-N60).<sup>98</sup>

In lower extremity SSEP, a prolonged N23-P31 (spinal cord conduction time) or N23-P40 (P37) (central conduction time) may be seen. Because N23 and P31 are not obligate potentials,



**Figure 4-32.** An example of an abnormal SSEP in a patient with a lesion affecting the VPL nucleus in the right thalamus. This patient had dense hemi-sensory deficit in left side. Right-sided stimulation was normal, but left-sided stimulation showed absence of all cortical potentials. Subcortical potentials, P14 and N18, and N13 (cervical potential) were normal. (From Yamada T, Dickins QS, Machida M, et al. Somatosensory evoked potentials to simultaneous bilateral median nerve stimulation in man: method and clinical application. In: Cracco RQ, Bodis-Wollner I, eds. *Frontiers of Clinical Neuroscience. Evoked Potentials*. Baltimore, MD: Williams & Wilkins, 1986:246–261, with permission.)



**Figure 4-33.** An example of an abnormal SSEP in a patient with a left parietal lesion. Bilateral stimulation revealed a clear asymmetry between CP3 and CP4 responses with delayed N20, P26, and N32 at CP3 electrodes.

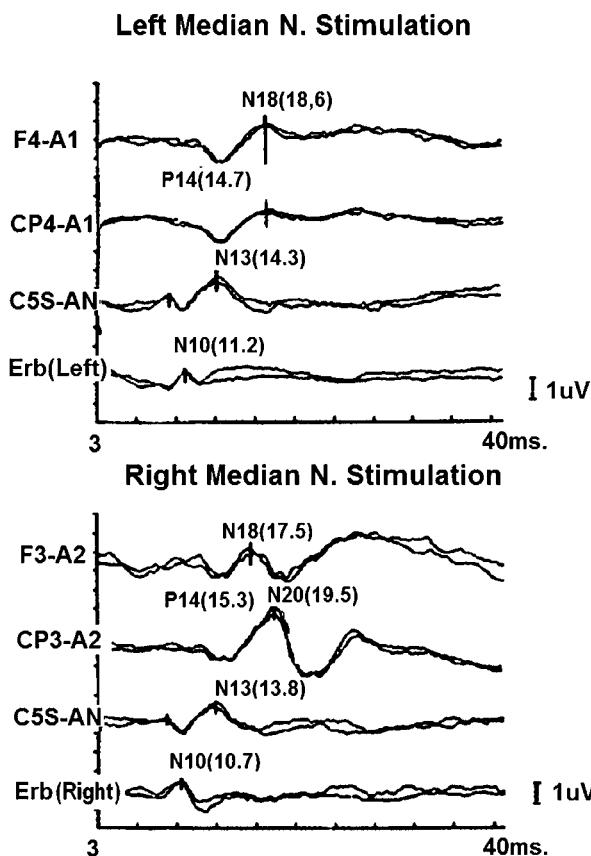
it is often not possible to differentiate if the abnormality is of central or peripheral origin in the lower extremity SSEP.

#### FRIEDREICH'S ATAXIA

Because in Friedreich's ataxia large-diameter fibers are primarily affected while sparing small-diameter fibers, the patients usually have a loss of vibration and position sensation and normal pain and temperature sensation. Due to large fiber involvement, SSEP often abnormally affects mainly N20 (cortical potential), either with a delayed latency or with a temporally dispersed waveform.<sup>99–101</sup> Erb's potential and cervical N13 are usually normal. This indicates a mainly central conduction abnormality. As the disease progresses, the peripheral sensory nerves may be affected, causing an abnormality starting at Erb's potential.

#### MOTOR NEURON DISEASE

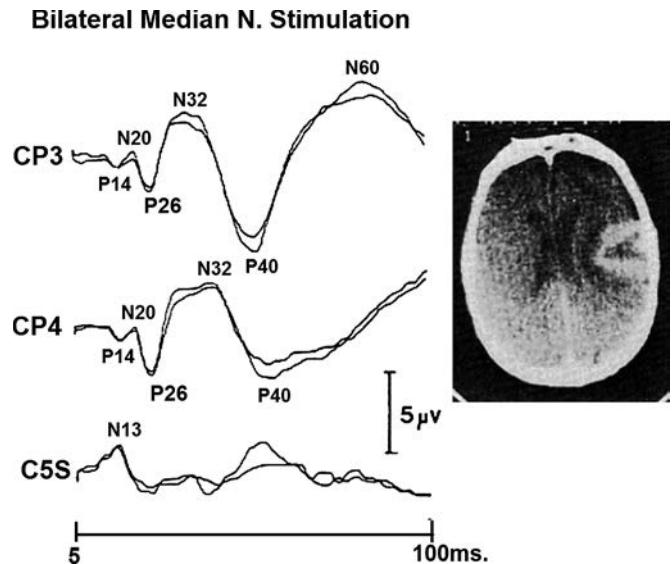
Amyotrophic lateral sclerosis (ALS) and other motor neuron diseases such as primary lateral sclerosis and progressive spinal



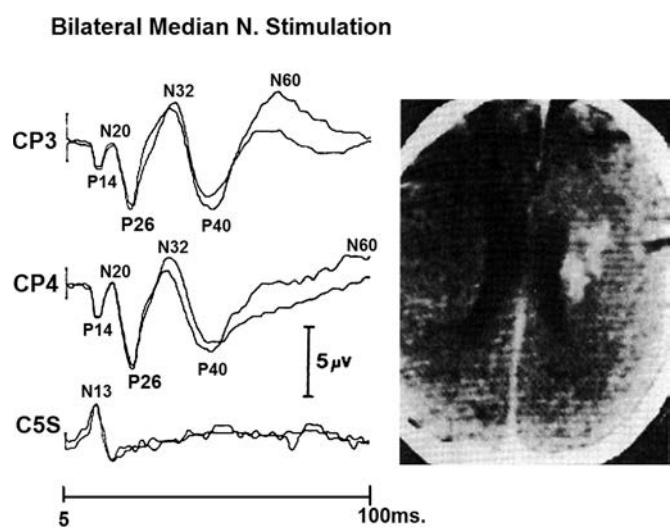
**Figure 4-34.** An example of absence of N20 but preserved N18 (subcortical potential). Right-sided stimulation showed normal N20 and N18 with a near-phase reversal between frontal and parietal electrodes. Left-sided stimulation showed a broad negative potential with the same latency at both the frontal and the parietal electrodes. This indicated that the negative potential after P14 was not N20 but N18. This SSEP suggested a possible lesion affecting the VPL nucleus of the thalamus or area 3b of the primary sensory cortex.

muscular atrophy mainly involve the motor system, mostly sparing the sensory system. However, some patients may have sensory deficits in the touch and pressure sensations.<sup>102</sup> The posterior columns are generally spared, but it may be involved in familial ALS patients. Reflecting these inconsistent sensory involvements, the reports of SSEP studies in ALS or other motor neuron diseases have been conflicting. Some studies have reported normal median nerve SSEP in most ALS patients<sup>103,104</sup>, while other studies showed abnormalities in cervical N13,<sup>105</sup> prolonged Erb's—N20 IPL or N13-N20 IPL.<sup>106,107</sup> Our earlier study showed abnormalities limited to longer latency components (N32, P40, N60) revealed by the asymmetric responses after bilateral simultaneous stimulation.<sup>108</sup> The results of tibial nerve SSEP have also been conflicting; some reported delayed cortical potentials,<sup>109</sup> or prolonged central conduction time,<sup>107</sup> while others did not.<sup>110</sup>

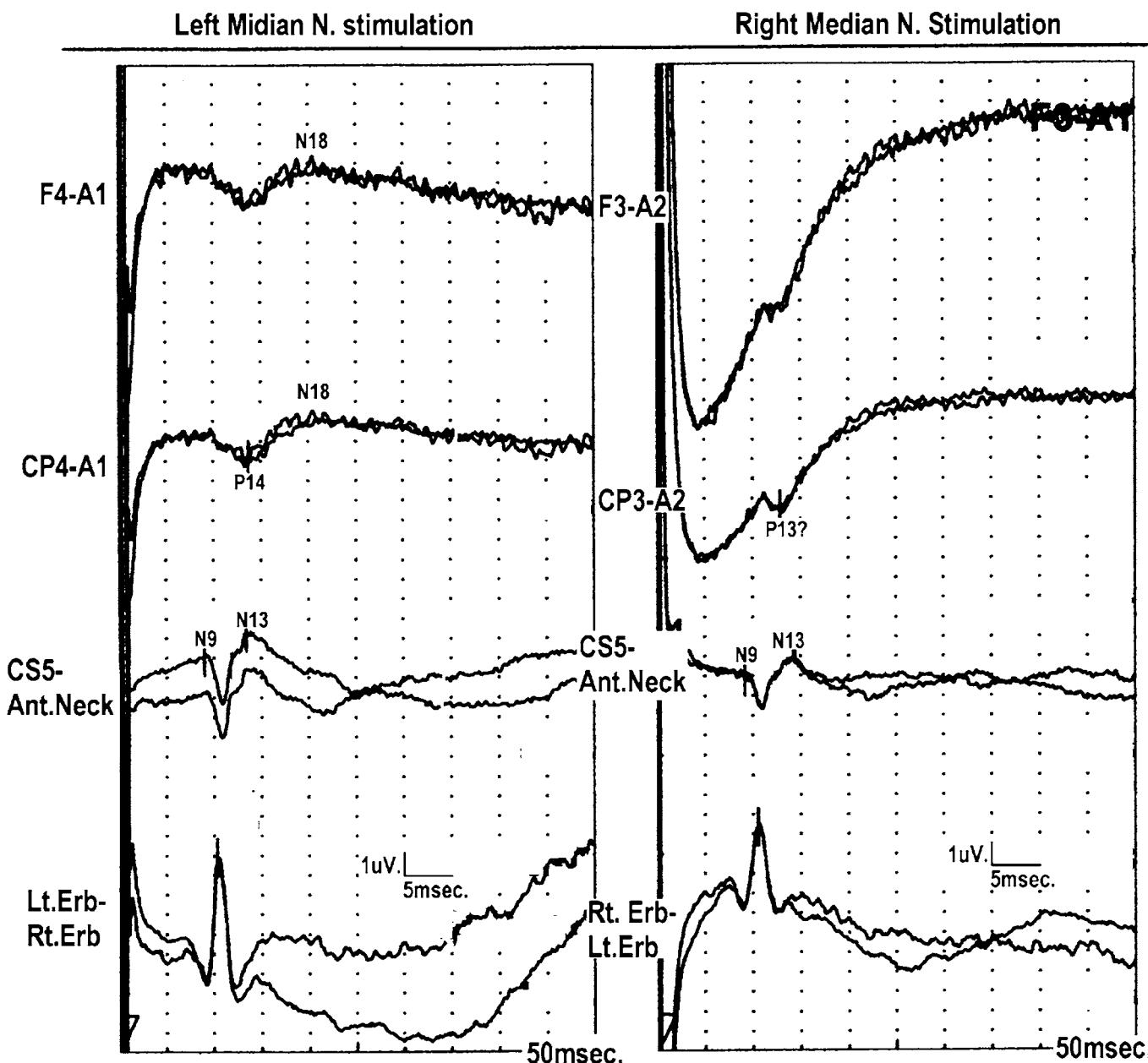
Because these SSEP abnormalities can be seen not only in motor neuron disease but also in patients with cervical cord myelopathy presenting with similar clinical symptoms,<sup>111</sup> it is important to exclude myelopathy before diagnosing a motor neuron disease.



**Figure 4-35.** An example of an abnormal SSEP affecting medium-latency components, leaving short-latency components intact, revealed by bilateral stimulation. Note the delayed N32 with delayed N60 at CP4 corresponding to the side of the lesion shown by CT scan. N60 was presumably delayed beyond the time scale of 100 msec. (From Yamada T, Dickins QS, Machida M, et al. Somatosensory evoked potentials to simultaneous bilateral median nerve stimulation in man: method and clinical application. In: Cracco RQ, Bodis-Wollner I, eds. *Frontiers of Clinical Neuroscience. Evoked Potentials*. Baltimore, MD: Williams & Wilkins, 1986:246–261, with permission.)



**Figure 4-36.** An example of an abnormal SSEP (revealed by bilateral stimulation) affecting only the N60 component at CP4 corresponding to the side of lesion (From Yamada T, Dickins QS, Machida M, et al. Somatosensory evoked potentials to simultaneous bilateral median nerve stimulation in man: method and clinical application. In: Cracco RQ, Bodis-Wollner I, eds. *Frontiers of Clinical Neuroscience. Evoked Potentials*. Baltimore, MD: Williams & Wilkins, 1986:246–261, with permission.)



**Figure 4-37.** An example of absent N20 bilaterally in a comatose patient after anoxic cerebral insult. The absence of N20 is indicated by the same waveform at Fc and CPc electrodes. The slow blunted potential is likely N18 after intact P14 on the left-side stimulation.

#### SPINOCEREBELLAR DEGENERATION

A relatively high incidence of SSEP abnormalities has been reported in this condition.<sup>112-114</sup> The abnormalities include depressed or absent N13 (cervical) and/or prolonged or depressed N20 (cortical potential).

#### HUNTINGTON'S CHOREA

All studies agree that the characteristic SSEP finding in Huntington's chorea is a marked amplitude reduction of the short-latency cortical potential in both median and tibial nerve SSEPs.<sup>115-118</sup> The amplitude reduction has also been observed in family members at risk.<sup>116,118</sup> It should be noted that low-voltage

activity is also a characteristic finding in EEG<sup>119-121</sup> and VEP in Huntington's chorea.<sup>122-124</sup>

#### COMA AND BRAIN DEATH

The median nerve SSEP is used not for evaluation of the sensory pathway but for prognostic assessment in comatose patients. The absence of N20 (N20-P26) bilaterally is a sensitive measure indicating a grave prognosis in comatose patient. With this abnormality, many studies agree that the incidence of death is greater than 80%. Less than 20% may survive, but with the vegetative state or severe disability.<sup>125-129</sup>

In order to determine the absence of N20, at least two scalp recordings are required because N18 may remain intact in

association with an absent N20 (intact N18 could be mistakenly identified as N20 if the presence of N18 is not verified by a separate channel). This can be accomplished by using one channel (CPi-Epi) to record all the FFPs including N18 and a second channel (CPc-CPi) to verify an absent N20. Alternatively, an absence of N20 can be demonstrated when negative potentials in both frontal (Fc) and parietal (CPc) electrodes have the same latency with the ear or noncephalic reference recording (Fig. 4-37; see also Figs. 4-32 and 4-34). In this case, the negative potential at CPc electrode is not N20 but an intact N18 after the deletion of N20.

In brain-dead patients, P14 and N18 FFPs and N20 should be absent but cervical N13 may be present.<sup>130-132</sup>

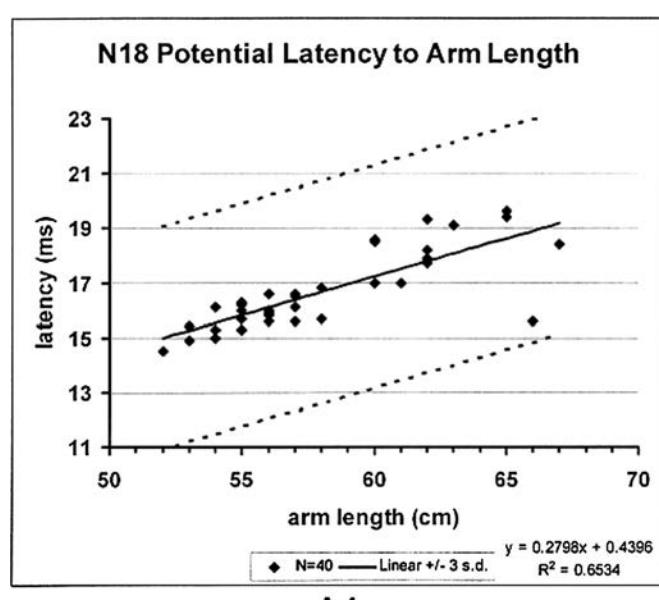
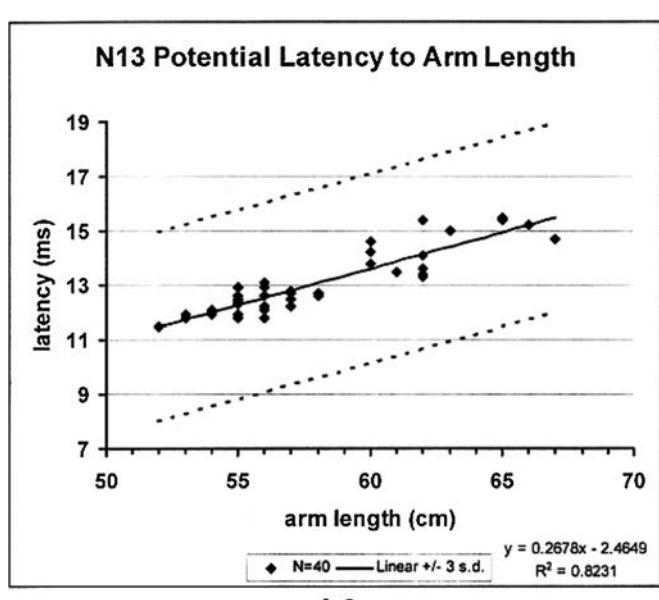
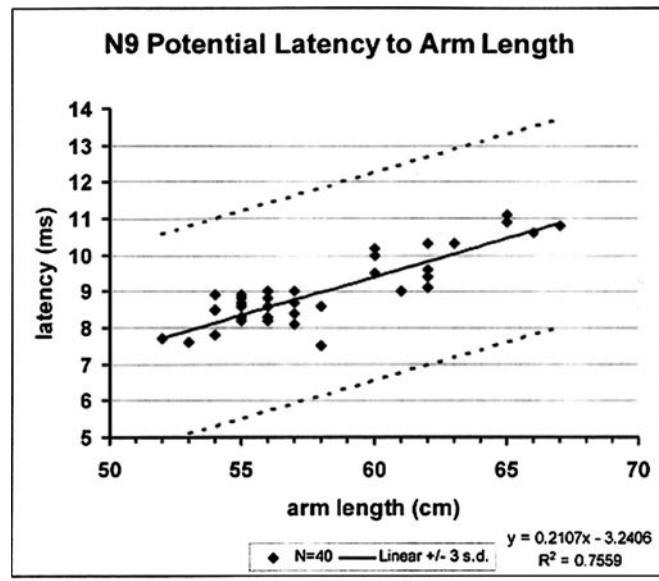
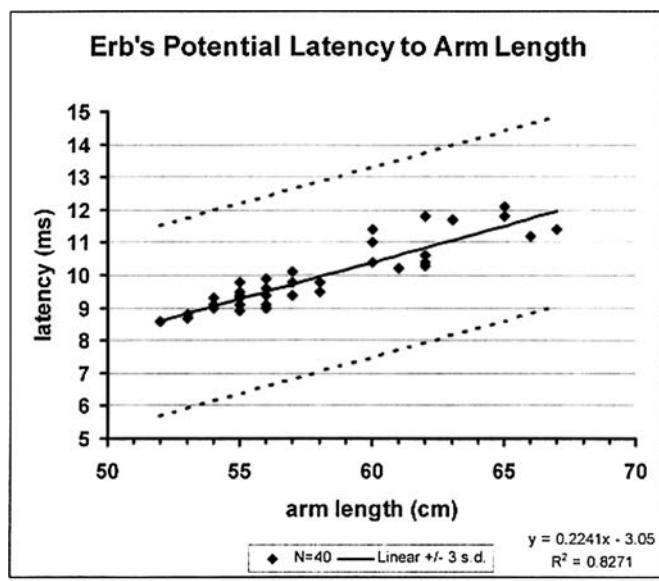
### MYOCLONIC EPILEPSY

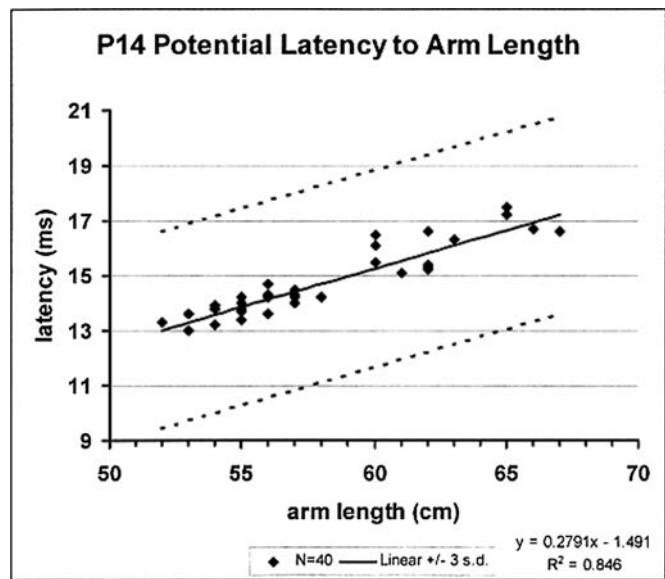
EP abnormalities in general are described by latency prolongation and/or amplitude depression. In contrast, myoclonic

epilepsy often shows a normal N20, but the amplitude of subsequent positive potential, P26, is markedly enhanced. This so-called giant SSEP was found in myoclonic epilepsy of various etiologies including Lafora body disease, Unverricht Lundborg disease,<sup>133,134</sup> lipidoses, neuronal ceroid lipofuscinosis, postanoxic myoclonus, and Creutzfeldt-Jakob disease.<sup>135,136</sup>

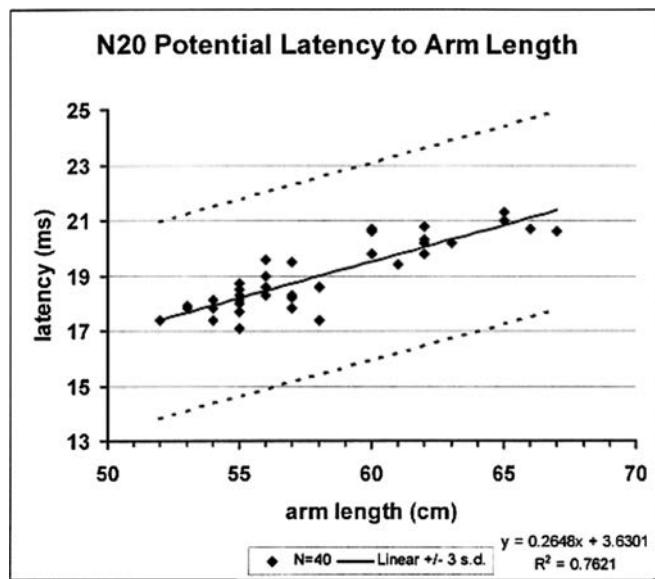
### APPENDIX FIGURES 4A-1 THROUGH 4A-12

Normal SEP components data shown by graphs in relationship with arm length for the median and height for the tibial nerve. (From Yeh M, Yamada T, Kimura J. Application of SSEP reading in the evaluation of the peripheral nervous system. In: Kimura J, ed. *Peripheral Nervous Disease, Handbook of Clinical Neurophysiology*, vol. 7. Elsevier, 2006:443–466, with permission.)

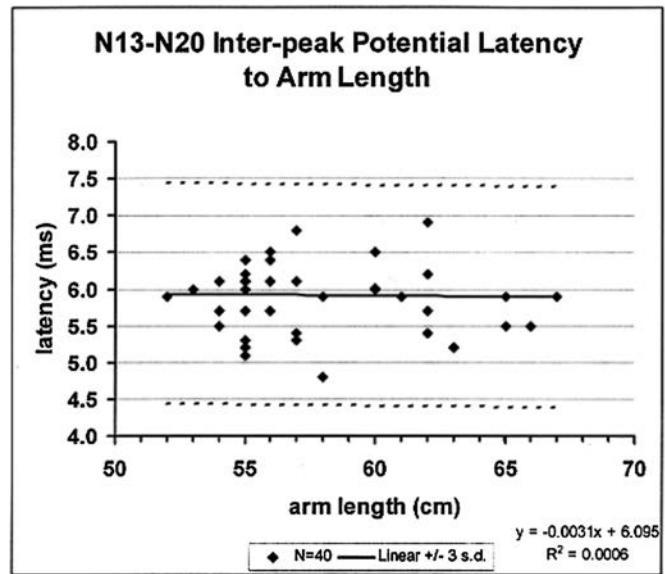




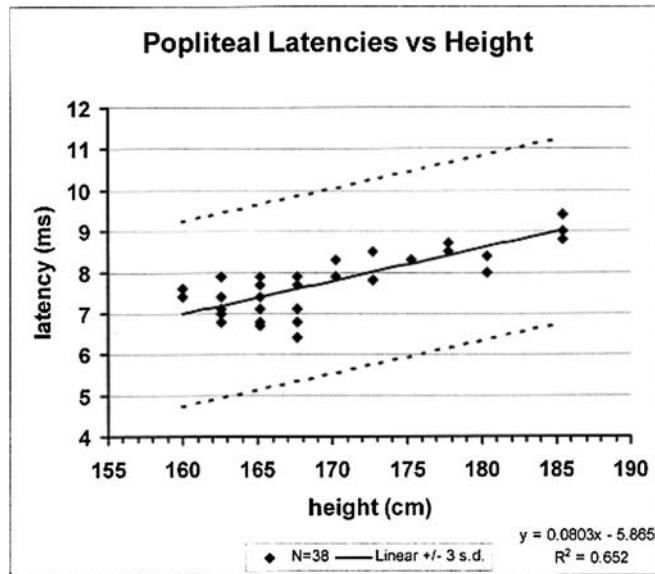
A-5



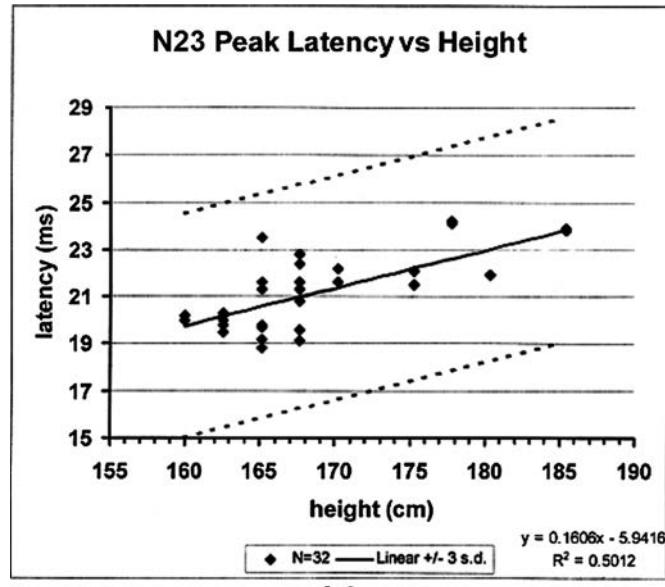
A-6



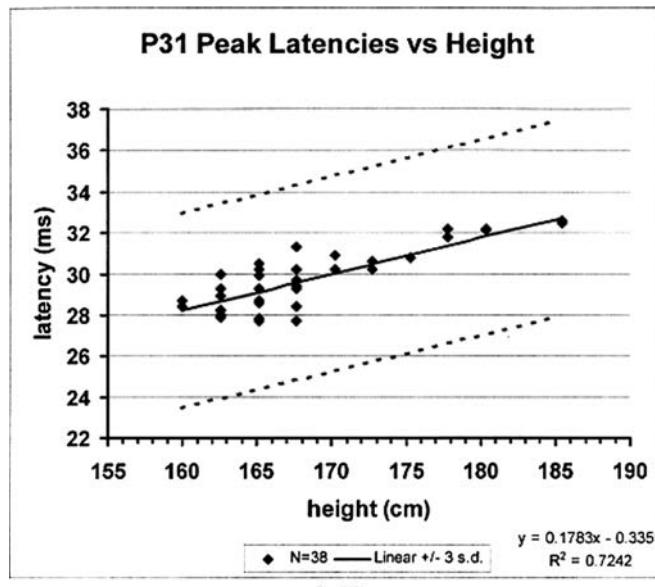
A-7



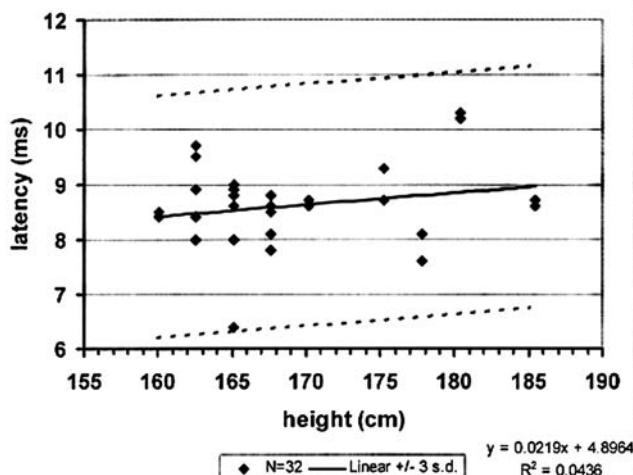
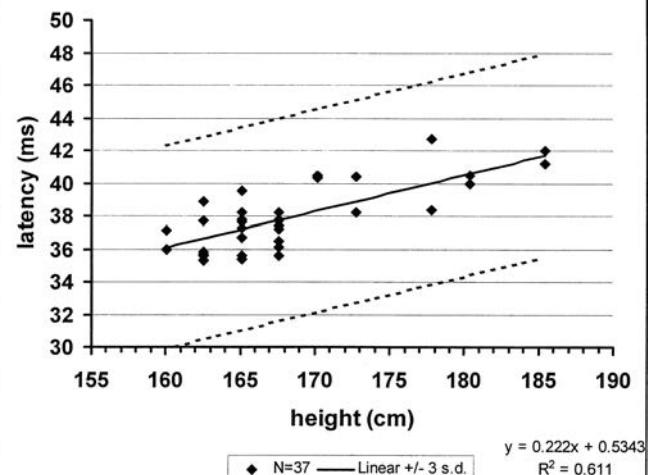
A-8



A-9



A-10

**N23-P31 Interpeak Latency vs Height****A-11****P40 Peak Latency vs Height****A-12****REFERENCES**

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## SECTION II

# Intraoperative Neurophysiologic Monitoring

CHAPTER

# 5

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## Introduction and Recording Technology

### ABBREVIATIONS

<b>ASET</b>	American Society of Electroneurodiagnostic Technologists
<b>NIOM</b>	Neurophysiologic Intra-operative Monitoring (used interchangeably with IONM)
<b>ABRET</b>	American Board of Registration of Electroencephalographic and Evoked Potential Technologists
<b>AAET</b>	American Association of Electrodiagnostic Technologists
<b>R. EEG T.</b>	Registered Electroencephalographic Technologist
<b>R. EP T.</b>	Registered Evoked Potential Technologist
<b>RNCST</b>	Registered Nerve Conduction Study Technologist
<b>CAAHEP</b>	Commission on Accreditation of Allied Health Education Program
<b>CNIM</b>	Certification in Neurophysiologic Intraoperative Monitoring
<b>EEG</b>	Electroencephalography
<b>EMG</b>	Electromyography
<b>BAEP</b>	Brainstem auditory evoked potential
<b>SSEP</b>	Somatosensory evoked potential
<b>MEP</b>	Motor evoked potential

<b>TcMEP</b>	Transcranial motor evoked potential
<b>CMAP</b>	Compound muscle action potential
<b>END</b>	Electroneurodiagnostic

### INTRODUCTION

Neurophysiologic intraoperative monitoring (NIOM) has become the standard of patient care regarding spine, spinal cord, and brain surgeries. As the number of NIOM cases increases, so does the need for qualified, educated, and experienced technologists. In this chapter, we will address the requirements for the NIOM technologist and some of the basic concepts for NIOM.

The NIOM technologist needs to have not only technical skills in recording the physiologic response but also knowledge concerning operating room procedures, anesthesia as well as neuroanatomy and neurophysiology. The technologist needs

be able to work closely with other health care providers in a professional manner.

The job description of the NIOM technologist published by ASET states that these individuals are specialists.<sup>1</sup> A Level 1 NIOM specialist must have an ABRET or an AAET credential (R. EEG T, R.EP T, CNIM or RNCST) plus completion of an electroneurodiagnostic program accredited by CAAHEP or a bachelor's degree or higher from an accredited college. Here, the title "specialist" is used interchangeably with "technologist."

Before surgery, the NIOM specialist is required to review the planned intraoperative procedure, evaluate the structures at risk, select the appropriate modality, make any necessary technical adjustments, and if necessary, communicate with the neurophysiologist, surgeon, or anesthesiologist. During the surgery, the NIOM specialist monitors the neurophysiologic function of the central and peripheral nervous systems, communicating with the neurophysiologist, surgeon, and anesthesiologist.

## **NIOM TECHNOLOGIST'S RESPONSIBILITIES AND SKILLS**

There are three main phases of neurophysiologic monitoring: preoperative, intraoperative, and postoperative.

### **PREOPERATIVE PREPARATION**

The NIOM technologist should be able to identify the anatomical structures at risk during specific surgical procedures, thereby being able to determine which modalities are most appropriate such as EEG, EMG, BAEP, SSEP, and/or MEP monitoring. Determining the modalities depends on the type of surgery. A preoperative workup including baseline studies and a review of the patient's medical history will help the technologist to determine if pertinent monitoring data can be gathered intraoperatively. For instance, if a patient has a diagnosis of neuropathy and a baseline somatosensory evoked potential (SSEP) shows decreased or no measurable response by conventional stimulus sites (wrist for upper and ankle for lower extremity SSEP), the technologist can then alter the monitoring plan to utilize stimulus sites such as the popliteal fossa (either peroneal or tibial nerve) for lower extremity SSEPs or the elbow (either ulnar or median nerve) for upper extremity SSEPs (see Chapter 16, Figs. 16-1 and 16-2). The same applies when the wrist or ankle is not accessible as a stimulus site due to a deformity or an injury. A check of the patient's medical history will also alert the technologist of latex allergies that could preclude the use of some standard supplies.

After the pertinent information is gathered, the technologist, along with the surgical team and neurophysiologist, can create an appropriate plan for the course of the surgery. Keeping the patient informed about the utility of the monitoring procedure will create a more relaxed and cooperative environment. The final step in preoperative preparation is to prepare reliable and efficient monitoring equipment and supplies (supplies will be discussed in greater detail in a following section). Understanding spinal cord systems and the modalities that protect those systems, the technologist can make a decision regarding the equipment that will be best suited for the surgery. An example would be to determine if the patient will be better served with SSEP or EMG monitoring. Monitoring equipment is often complex and can be made with multimodality capabilities. The many instrument

components include input and stimulus cables, electrode junction box, computer, cameras, speakers, networking access, etc. The technologist must be able to navigate thorough all these components before the monitoring can begin.

### **INTRAOPERATIVE PHASE**

The intraoperative phase of monitoring begins when the technologist enters the operating room. Setting up the equipment and preparing the patient with appropriate electrodes (recording/stimulating) is the first step of intraoperative monitoring. Care must be taken to ensure electrical safety. The technologist should also confirm that the modalities chosen are appropriate for the surgical plan. Electrodes should be applied securely and safely to optimize the monitoring technique.

After a plan is established and the recording and stimulus parameters are set, the monitoring can begin. During monitoring, the technologist must constantly evaluate the averaging process and the evolution of the waveforms by comparing the new response with the previous one and also with the baseline responses. The technologist must be able to identify waveforms specific to the chosen modality; for example, P14 and N20 for upper extremity SSEP and P31 and P40 for lower extremity SSEP (see Figs. 4-8, 4-13, 4-19, and 4-23). The technologist must also know when changes are significant enough to alert the neurophysiologist/surgical team. This is determined by using alarm criteria. When changes in the response meet the alarm criteria, the neurophysiologist/surgical team can be alerted promptly so as to avoid possible neuronal injury. The technologist must be constantly aware of what the surgeon is doing in order to modify the test as needed or judge if the changed waveform is clinically significant. For example, responses can be noisy or lost when the surgeon is using cautery. A MEP can be totally lost when a muscle relaxant is used. Peak latencies may become prolonged purely because the surgeon irrigates the surgical site with cold water, especially during BAEP monitoring. The alert technologist, knowing what is going on in the surgery, will recognize these types of changes for what they are rather than as a sign of impending neuronal damage.

Another key role for the technologist is to communicate with all the staff involved in the care of the patient including surgical, anesthesia, nursing, and neurophysiology staff. All changes in the anesthetic and surgical course must be relayed to the technologist for documentation. The intraoperative phase ends when the surgical staff has confirmed that they are no longer putting neurological systems at risk and/or the operation is complete. At this time, it is the technologist's responsibility to remove all monitoring supplies from the patient and either disinfect or dispose of them properly per laboratory protocol.

### **POSTOPERATIVE PHASE**

Often, the technologist continues to monitor throughout closing till the patient is ready to be moved or extubated. Removal of needle electrodes should be done carefully so as not to disturb IV or arterial lines, or cause a needle stick to yourself or other OR personnel. Disposable stick on electrodes can also be removed at this time. After monitoring is completed, the monitoring equipment itself must be cleaned and any necessary maintenance should be performed prior to the next surgical case. Restocking of the supplies kept with the monitoring

equipment would also be prudent. Finally, all reports and documentation should be available for review by the interpreting physician and other staff involved in the patient's care. It is important that patient confidentiality be maintained at all times and the code of ethics be followed.

## EQUIPMENT AND SUPPLIES

In order for a procedure to run smoothly, the technologist must be fully trained and comfortable with the monitoring equipment. Many manufacturers now offer NIOM equipment that is made with a multitude of features such as multimodality capabilities. Most monitoring equipment has the ability to run SSEP, BAEP, MEP, EMG, and even EEG during the course of a surgery.

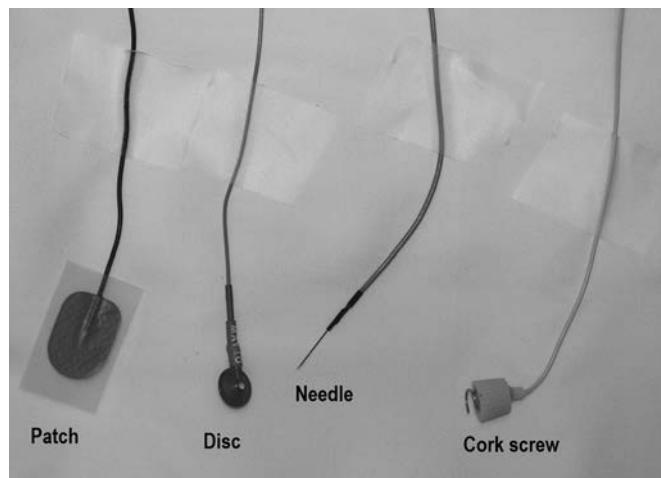
There are several factors to consider when choosing an instrument for NIOM. The technologists in your laboratory may have differing levels of computer skills, so choosing an instrument that is user friendly and has adequate technical support with training opportunities should be taken into consideration.

Gathering the necessary supplies is also very important. The supplies will vary depending on the type of procedure being performed and the modalities being utilized. Certain provisions, like electrodes, tape, and skin preparation materials, are always necessary. Electrodes come in many shapes, sizes, and colors and can be provided by numerous companies (Fig. 5-1). Traditional EEG disc electrodes can be used on the scalp, but the application takes longer and the impedance is higher than needle electrodes. For this reason, subdermal needle electrodes are most commonly used in NIOM monitoring. Electrodes found in the needle category are usually made of stainless steel or platinum, and they are disposable and packed in sterilized packaging. Care must be taken when placing and removing these electrodes. The skin must be cleaned before placement to avoid infection. To avoid needle sticks from contaminated needle electrodes, careful removal and proper disposal are vital. Recently, corkscrew-type electrodes have been used, which are more securely attached to the scalp than needle electrodes. They can be used as recording electrodes for SSEP as well as stimulating electrodes for TcMEP. Needle and corkscrew electrodes are applied after the patient is anesthetized.

Another common electrode utilized in operating room monitoring is the self-adhesive surface electrode that can be used to stimulate peripheral nerves as well as to record TcMEP or CMAP (Fig. 5-1). These electrodes generally have a surface area of approximately 20 mm<sup>2</sup>. They are pregelled with electrolyte, composed of silver/silver chloride, and disposable. Self-adhesive electrodes have the advantage of being noninvasive and there is no risk to the technologist or the patient; however, the impedance of these electrodes tends to be higher than that of needle or disc electrodes.

Another type of surface electrode essential to monitoring is the ground patch/electrode. Although very similar in composition to the recording/stimulating electrodes, they usually have a larger surface area. The purpose of a grounding electrode is to eliminate 60-Hz artifact that is abundantly present in the operating room. It will also help to reduce stimulus artifact.

All these electrodes come in many shapes and sizes, and the technologist has to decide which works best for their laboratory



**Figure 5-1.** Four different types of electrodes.

protocols. It would also be prudent to be well prepared for any unforeseen circumstances that may arise in the operating room. Equipment can malfunction; cables can be broken or disconnected. It is up to the technologist to identify the potential problems and have backup supplies and equipment to replace them.

The technologist is not responsible for the interpretation of data. The final interpretation is done by an experienced neurophysiologist. It is rare for such personnel to directly supervise in the operating room and, therefore, having networking capability (remote access) on the monitoring equipment to send online data is essential to communicate with the neurophysiologist remotely.

## SOMATOSENSORY EVOKED POTENTIALS

SSEPs are one of the oldest and most commonly used procedures for NIOM. They are now used in conjunction with other modalities such as TcMEPs. SSEPs are commonly used in spine and spinal cord cases like intra/extramedullary tumors, syrinx, surgical treatment of scoliosis, thoracoabdominal vascular surgery, tethered cord syndrome and fusions (cervical, thoracic, and lumbar) with instrumentation and manipulation. Most of the procedures explained here are based on current clinical practices and articles.<sup>2-6</sup>

SSEPs are recorded by electrically stimulating the peripheral sensory nerves and recording with surface or needle electrodes placed on the surface over the peripheral nerve, spine, and scalp.

The median or ulnar nerve is stimulated at the wrist for upper extremity SSEP monitoring, and the posterior tibial nerve is stimulated at the ankle for lower extremity SSEP. The peroneal nerve at the knee can be used if the posterior tibial nerve is not accessible, but this results in vigorous leg movement that may interfere with the surgical procedure.

When planning NIOM using SSEPs, it is preferable to obtain a preoperative baseline. The study is done prior to the surgery in the clinical END laboratory using standard four-channel SSEP protocol (see Figs. 7-2 and 7-4; see also Figs. 4-13 and 4-23). This allows the opportunity to meet the patient, review

the medical history, check the instrument, and make an appropriate intraoperative monitoring plan. To avoid unexpected adverse circumstances in the operating room, document any clinically significant information about the patient, that is, peripheral neuropathy, missing extremity, or any other neurological disease. An absent or a nonmeasurable preoperative baseline response recorded in the awake state does not preclude successful NIOM; it is not uncommon to see a well-defined response obtained under anesthesia despite poorly recognized preoperative baseline responses recorded in the awake state. This is because under anesthesia muscle or movement artifacts are absent and the stimulus intensity can be increased beyond the degree tolerable to an awake patient.

The technologist applies recording and stimulating electrodes to the patient in the operating room suite, securing them in place. Stimulus cables can be as long as 3 m, allowing the technologist to plug in all the stimulators at the head of the bed where they are easily reachable during the case if there is a need to troubleshoot.

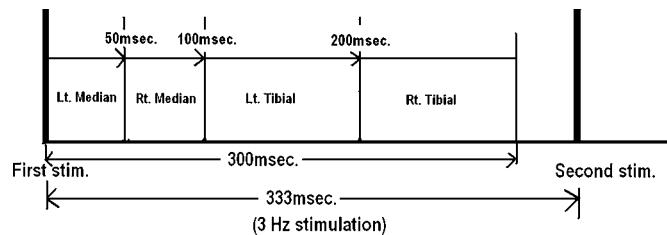
Disposable stick on electrodes are placed at the popliteal fossa to record the peripheral nerve action potential following posterior tibial stimulation and also at Erb's point bilaterally to record the ulnar or the median nerve response. Sometimes, Erb's point is not accessible, especially in an anterior cervical case. In this case, the peripheral recording electrodes could be placed at the elbow (ulnar groove for ulnar and medial aspect of elbow for median nerve stimulation). After the electrodes are placed, they are covered with an adhesive tape to secure them in place. The peripheral channels may not always be displayed during monitoring but should be available if the technologist needs to check the integrity of stimulus delivery while troubleshooting.

Instead of disc electrodes used for diagnostic SSEP, disposable subdermal needle electrodes are generally used in NIOM because the needle electrodes have lower impedance and are easier to apply. There is no discomfort to the patient if these electrodes are applied under anesthesia. They are placed at CPz, CP1, CP2, CP3, and CP4; FPz (Fz), A1, A2, and ground. CP3 and CP4 are used for upper extremity SSEP and CP1, CP2, and CPz electrodes are used for lower extremity SSEP with references at A1, A2, and Fpz (see Figs. 4-13 and 4-23; also see Figs. 7-2 and 7-4). Redundant or backup electrodes are useful in case an electrode is lost during the surgery. More than likely, a needle can be reinserted after it has been dislodged.

The stimulations are delivered to all four extremities in a sequence. With a window of 50 ms for upper and 100 ms for lower extremity stimulations (a total window length of 300 ms for all four extremities), stimulus rates up to 3 Hz can be delivered (without overlapping windows) to the left and right upper and to the left and the right lower extremity nerves (Fig. 5-2).

With a stimulus duration of 200  $\mu$ s, the stimulus intensity can be up to 30 mA for uppers and 50 mA for lowers without causing an adverse effect. This is substantially higher than intensities used in a diagnostic SSEP on awake patients, which are usually about 10 to 20 mA. The increased stimulus intensity guarantees supramaximal stimulation (see Figs. 4-2 and 4-3).

A high filter of 500 to 1,000 Hz and a low filter of 10 to 30 Hz are commonly used. Because NIOM is done in an electrically "hostile" or "noisy" environment, relatively narrow filter settings such as 30 Hz for low and 500 Hz for high filter produce "cleaner" responses. Once filters are established, they should only be



**Figure 5-2.** Schematic model of four different stimulations in a series as an example using 50 ms window for left and right upper extremity stimulations and 100 ms window for left and right lower extremity stimulations. With this stimulus parameter, the fastest stimulus rate would be 3.3 Hz (1,000 ms/300 ms).

changed with the knowledge that changing filter settings may affect peak latency. The sensitivity setting can be adjusted such that 10% to 20% of the samples are rejected. If the sensitivity is set too low, samples including excessive artifact will be accepted, but if the sensitivity is set too high, all samples could be rejected. Generally, a sensitivity of 20  $\mu$ V works well. In total, usually 500 to 1,000 trials are averaged; if the response is "noisy," a greater number of averages are required, while a high amplitude and well-defined response requires fewer samples to be averaged.

Once the patient has been positioned and a preoperative baseline is obtained, the level of anesthesia, blood pressure, and temperature should be documented. In some cases, the surgeon may request a prepositioning baseline response, especially in patients with unstable cervical spine. In these patients, simple extension or flexion of the neck (which could be the result of positioning) may cause cervical spinal cord injury.

The preopening baseline is utilized throughout the procedure, acting as a control for comparing current data. A trending program helps to recognize progressive changes during the procedure. The baseline response can be displayed along with the trending data for comparison (Fig. 5-3).

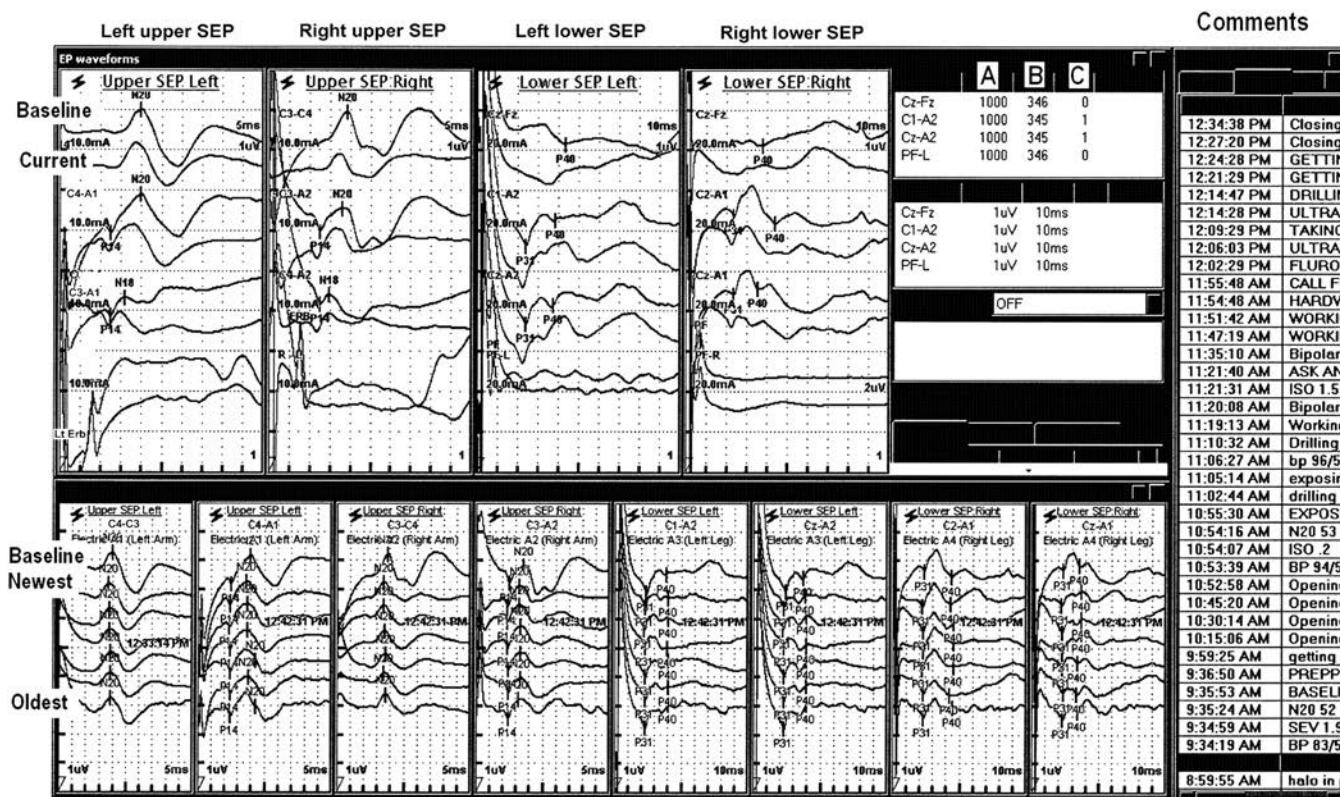
It is important to document any clinically significant events or changes during the procedure such as anesthesia levels, blood pressure, temperature, operative phases, and any other variable that might affect the tracings (see Fig. 5-3). Document these variables at least every 5 minutes during critical parts of the surgery and every 10 minutes during noncritical periods.

## ALARM CRITERIA

The technologist should alert the neurophysiologist promptly when there is a change in response. It should be verified that the change is clinically significant and not due to technical or noncritical issues before informing the surgeon of the change. Although there is a lack of precise data on alarm criteria, or warning signs of impending neural damage, it is arbitrarily and generally accepted that a 50% amplitude reduction and/or 10% latency increase are considered to be significant findings.

## TRANSCRANIAL MOTOR EVOKED POTENTIALS

TcMEPs are often used in conjunction with SSEPs to assess spinal cord function during surgery. While SSEP evaluates the ascending sensory pathway mediated through the posterior-spinal cord (dorsal column), TcMEP evaluates the anterior



**Figure 5-3.** An example of ongoing tracings during the SSEP monitoring.

portion of the cord or descending motor pathways (see Fig. 4-1).<sup>2-4,6</sup> Indication for TcMEP is the same as SSEP monitoring, but TcMEP is especially important for spine/spinal cord surgery using an anterior approach. Whenever possible, both SSEP and TcMEP should be monitored in any spine or spinal cord surgery.

Because utilization of TcMEP as a surgical monitoring technique is relatively new, no solid standard has been established; thus, the recording protocol may vary from one laboratory to another.

TcMEPs are elicited by stimulating the scalp with a high-voltage stimulus and recording the CMAP (compound action potential) or MEP (motor evoked potential) from the muscles of the upper and lower extremities (Fig. 5-4; see also Fig. 7-7). The stimulating electrodes can be placed at C3 and C4 or C1 and C2. Although the stimulus sites at C3 and C4 elicit MEPs in both upper and lower extremity muscles, the most appropriate sites for stimulation are not certain; sometimes, adjusting the sites of stimulating electrodes may be necessary to obtain optimal MEPs. Once an appropriate site has been chosen, leave the stimulation electrodes in that location for the remainder of the case. Subdermal needle electrodes or corkscrew-type electrodes can be used for stimulation. A larger ground patch should be placed between the stimulus site and the recording electrodes, perhaps on the shoulder. One scalp electrode will be connected as an anode (positive polarity) and the other as a cathode (negative polarity). Anodal stimulation will result in MEP responses predominantly from the muscles in the opposite extremities, that is, C4 anode (positive) resulting in left-sided responses (see Fig. 5-4). However, it is not uncommon to elicit MEPs on both left and right extremities simultaneously (see Fig. 7-7)

The stimulus is given by a device capable of delivering a high voltage (up to 1,000 V). A train of three to five with an inter-stimulus interval (ISI) of 1 to 2 ms is more effective in eliciting MEPs than a single stimulus. Usually more than 200-mA intensity is required to yield measurable MEPs. Generally speaking, a voltage of 400 to 600 V delivers current of about 500 to 600 mA. The lower the stimulus electrode impedance is the less voltage is required to achieve a certain current intensity. Filter settings of 10 Hz for low and 1,000 Hz for high filter are appropriate, but narrower band width filters may be acceptable. The waveforms vary from one case to another and no standard waveforms are established. The waveforms would also vary depending on the locations of recording electrodes. The MEPs obtained after stabilized anesthesia serve as the control or the baseline waveform. A window of 70 to 100 ms will cover both upper and lower extremity MEPs. The onset latency of MEP is about 15 to 30 ms for upper and 30 to 60 ms for lower extremity muscles. The onset latency may vary depending on the arm length or height differences and also locations of recording electrodes.

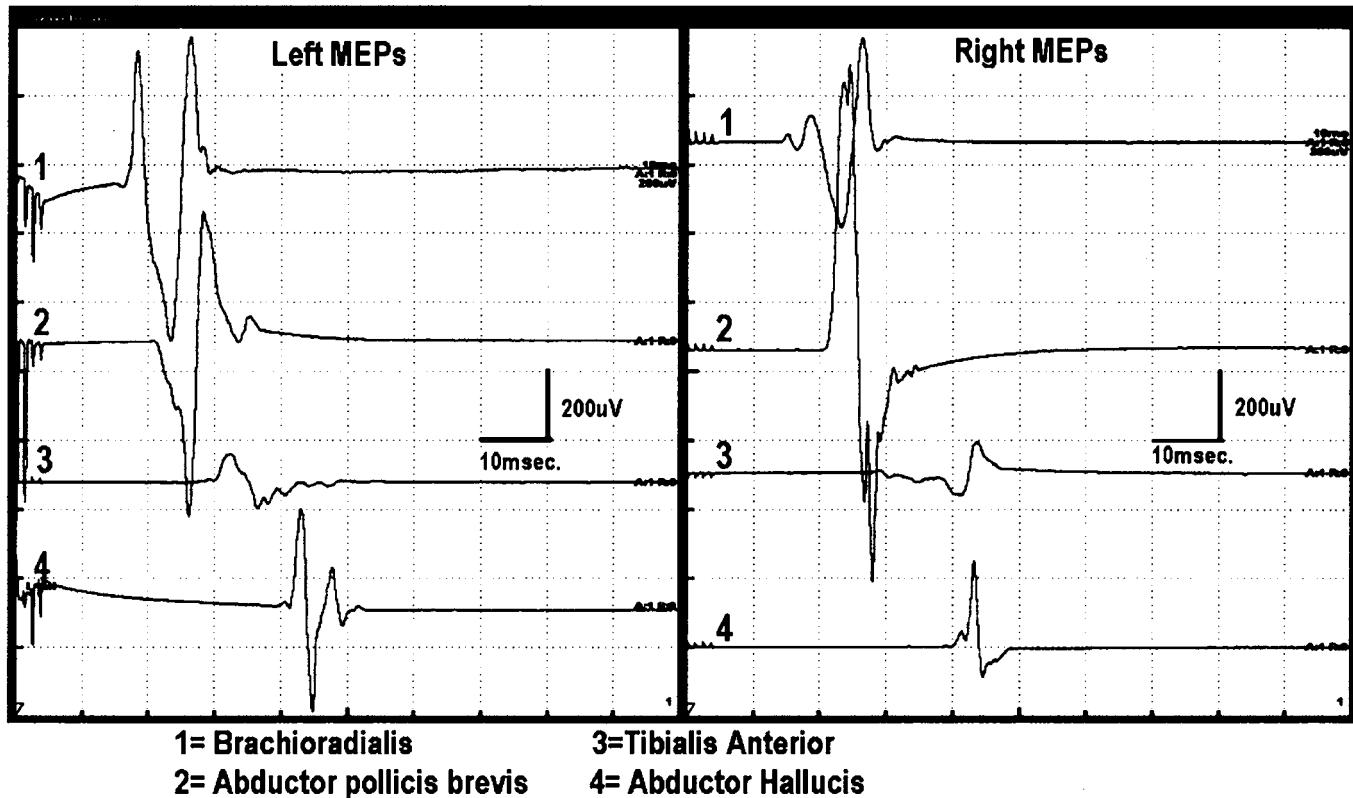
For recording electrodes, subdermal needles covered with adhesive tape may be used. The active electrode should be placed on the belly of the muscle with the reference electrode placed at least 3 to 4 cm away. Generally, two muscles from the upper and two muscles from the lower extremities are chosen [for upper extremities, brachioradialis (myotome C5, C6) and abductor pollicis brevis (C7, C8, T1), and for lower extremities, tibialis anterior (L4, L5) and abductor hallucis (S1, S2) muscles]. Smaller muscles generally produce a robust TcMEP. Ideally, the first TcMEPs should be performed once the patient has been anesthetized and intubated. But, the anesthesiologist will routinely use a muscle relaxant for intubation and this makes it

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**Stimulus parameters: 4 pulses (ISI=1msec)  
with 500volt (650mA)**

**C3=negative, C4=positive**

**C3=positive, C4=negative**



**Figure 5-4.** An example of MEP recorded from four muscles (two from upper and two from lower extremities) after four pulse trains of transcranial electric stimulation. Note positive stimulus polarity dictates the side of brain stimulation (anodal stimulation).

difficult to record a baseline MEP immediately after intubation. Once the muscle relaxant has worn off, the first TcMEP should be performed to test the integrity of the electrodes and stimulators and to obtain a baseline (control) MEP.

A soft bite block should be placed in the patient's mouth before MEP monitoring begins to prevent oral injury due to teeth clenching by stimulus delivery. Verify with the anesthesiologist that this has been done. Start with a stimulus of 100 V and work your way up in increments of 100 V until you have obtained measurable responses. Warn the surgeon and other operating room staff prior to stimulation since this may cause a jerky movement by the patient. Some surgeons may request TcMEP monitoring be performed only at specific times during the procedure. Once the surgeon has the spine exposed, TcMEPs should be performed about every 2 to 5 minutes, alternating with SSEPs.

No muscle relaxants should be used during MEP monitoring. All halogenated inhalation agents attenuate or abolish evoked potential waveforms and prolong latencies. (see section on anesthesia in this chapter and also Chapter 7). TcMEPs are far more sensitive to anesthesia than SSEPs. Constant communication

with the anesthesiologist is necessary to perform adequate TcMEPs.

#### ALARM CRITERIA

Although 50% amplitude reduction has generally been considered to be a warning sign, this is arbitrary and no solid data support this criterion. The inconsistency and variability of MEPs, which are far greater than SSEPs, pose more difficulties. The complete absence of MEPs for the first time after previously well-defined responses is not sufficient evidence to indicate warning. The warning to surgeons can be given only after the consistent absence of a response is verified and all possibilities of technical or systemic variables (anesthesia, blood pressure, temperature, etc.) are excluded. The unilateral loss of MEPs or dissociated loss of MEPs between upper and lower extremities is a more reliable finding for warning.

#### CONTRAINDICATION

Every NIOM laboratory has its own set of contraindications for TcMEPs. These should be well thought out and agreed upon by

the surgeon and the neurophysiologist before surgery. Generally speaking, the application of TcMEPs is avoided in patients with a verified seizure history or high seizure possibility secondary to neurological disorder. A patient who has metallic substances in the head or the face is also excluded. In patients who undergo high cervical spine or skull base surgery, special care must be taken because a neck or head jolt associated with the stimulation may interfere with the surgical procedure or may even cause spinal cord damage. In such cases, it is necessary to obtain permission from the surgeon and the surgeon must be clearly warned before delivery of stimulation. There should be communication with the surgeon prior to the case to make sure he has no objections to using TcMEPs. Sometimes, the surgeon prefers to use a muscle relaxant, for easier manipulation of the spine, rather than TcMEPs.

## PEDICLE SCREW MONITORING

Because SSEPs and MEPs involve multiple segments of nerve roots, they are not sensitive for detecting individual nerve root injury that may occur during thoracic or lumbosacral surgeries.<sup>7</sup> In order to prevent nerve root injury, pedicle screw monitoring is applied alone or in conjunction with SSEP or MEP monitoring. There are several indications for the use of instrumentation such as for correcting a deformity like scoliosis or spinal fusion for correcting a fracture of the spine. Pedicle screws are used in conjunction with other instrumentation (rods and plates) during spinal fusion to immobilize and realign the spine.

As the name suggests, screws are placed into the pedicle of the vertebrae to anchor the other instrumentation being used. If the screw is placed improperly, it can breach the pedicle wall and the nerve root may become irritated causing pain or in severe cases even damage the nerve (see Fig. 7-13). When nerve roots are irritated, the muscles innervated by that nerve root will also become irritated and activated, causing "neurotonic" discharges (see Fig. 7-14). By placing needle electrodes into the muscles associated with the level of surgery, EMG activity can be recorded (free-run EMG) and monitored for nerve root irritation or impending nerve damage.

Preoperatively, the technologist must know the level of the surgery and what muscles correspond to the nerve root to be examined. It is recommended to monitor one level above and below the planned surgical site in order to allow for changes in the surgical strategy.

Proper placement of the electrodes is crucial for an effective intraoperative monitoring. The best access to the patient will be before positioning. The skin must first be prepped with a sanitizing agent such as alcohol for infection control. The recording electrode should be placed into the belly of the muscle with the reference electrode about 3 to 4 cm away. The recording electrodes are not surface electrodes but must be inserted into the muscle tissue and correct insertion to the belly of muscle is crucial for appropriate CMAP recording. A ground electrode should also be used and placed between the stimulus and the recording electrodes, preferably on a bony surface such as the iliac crest. The electrodes should be secured in place with adhesive tape to make sure they remain in place throughout the entire surgery. The following table shows muscles and corresponding levels of spine.

• Adductor Longus	• L2, L3, L4
• Vastus Lateralis/Medialis	• L2, L3, L4
• Tibialis Anterior	• L4, L5
• Peroneus Longus	• L5, S1
• Medial Gastrocnemius	• S1, S2
• Rectus Abdominis Upper	• T5, T6
• Rectus Abdominis Middle	• T7, T8
• Rectus Abdominis Lower	• T9, T10, T11
• External Oblique	• T12
• Internal Oblique (Psoas)	• L1
• Trapezius	• C3, C4
• Biceps/Deltoid	• C5, C6
• Flexor Carpi Radialis	• C6, C7
• Triceps	• C6, C7, C8
• Abductor Pollicis Brevis	• C7-T1

After the surgeon has placed screws into the pedicle, it is time to see if the stimulus evokes an EMG (CMAP) response. A stimulus is delivered to the exposed portion of the screw via a ball tip probe that can either be directed by the technologist or the surgeon. If the pedicle wall is compromised, the stimulus will reach the nearby neural structures eliciting a CMAP in the corresponding muscle (see Fig. 7-13). The stimulus intensity is progressively increased from 0 to 30 mA. A screw is said to "pass the test" if at least 10 mA is reached without a response. It is considered to be "safe" if there is no response with stimulus intensity greater than 8 mA. If a response is elicited at less than 8 mA, the screw position must be adjusted or redirected to avoid nerve root irritation or damage.

It is possible to damage nerve roots during multiple parts of the surgical procedure such as decompression or instrumentation. Free-run EMG can be used during any process that puts a nerve root at risk. The spontaneous EMG activity can be viewed on a video screen and/or heard through an audio speaker. A prolonged burst (>10 seconds) of EMG activity (neurotonic discharge) suggests impending nerve damage and warns the surgeon so that adjustments can be made to the surgical maneuver (see Fig. 7-14).

Commonly used recording parameters are a band pass of 10 to 3,000 Hz, sensitivity of 50 to 100  $\mu$ V, and analysis time of 300 to 2000 ms for free-run EMG and 100 ms for evoked EMG.

## BRAINSTEM AUDITORY EVOKED POTENTIALS

Brainstem auditory evoked potentials (BAEPs) have been applied for surgical procedures involving the brain stem or the skull base. It is commonly used for cerebellopontine angle tumors like acoustic neuromas.<sup>8</sup> Other indications include microvascular decompression for trigeminal neuralgia or hemifacial spasms.<sup>9</sup> BAEP monitoring is often combined with EMG monitoring of various cranial nerves. The details of cranial nerve monitoring are beyond the scope of this chapter. (Additional information may be found in Brown and Veitch (1994).<sup>10</sup>) The BAEP recording concept in the operating room is similar to that of a BAEP in the diagnostic laboratory (see Chapter 3 for further detail). Some of the techniques vary to accommodate the operating room environment. An example is the stimulation technique. In the laboratory, headphones are commonly

used and in the operating room ear phones inserted in the external ear canal are used. Ear phone inserts are applied after the patient is prepared and in position. This way they will not be dislodged while moving the patient. The insert is placed in the ear canal; cotton is positioned around the tube, ensuring that it is not kinked or blocked in any way. A water-proof adhesive is applied over the ear protecting the insert from moisture and securing it in place. Cz is used for an active electrode and the references are on each ear lobe or mastoid. The ground electrode can be placed on the forehead.

Recording parameters include a high filter of 3 kHz and a low filter of 10 Hz, with a sensitivity of 20  $\mu$ V. The montage is Cz-A1 and Cz-A2. BAEP waveforms are often expressed “positive up,” which is opposite to VEP or SSEP. Because the polarity expression of EP instruments may differ depending on the model, the technologist must know the polarity convention of each instrument. If the EP instrument is made as “positive up,” Cz should be connected to input 1 and A1 or A2 must be connected to input 2 in order to express “positive up.” If the EP instrument is made “positive down” like an EEG machine, the Cz and A1 or A2 inputs must be reversed.

The stimulus rate can be faster than the 11 Hz generally used for diagnostic recordings. 20 to 30 Hz is appropriate, which allows faster data collection. Several hundred to thousand responses are required to record a reliable response. A click intensity of 105-dB PeSPL can be used without risk of hearing loss for anyone above the age of 10 years. For patients younger than 10, the intensity should be decreased accordingly to prevent auditory nerve damage by prolonged exposure of loud clicking sounds. The technologist can use rarefaction, condensation, or alternating clicks, whichever provides the best recording.

### **ALARM CRITERIA**

Because wave V is the most consistent and readily identifiable component, wave V is primarily followed during surgery. BAEP is quite sensitive to surgical maneuvers such as irrigation with cold water or stretching the auditory nerve. Unlike SSEPs or MEPs, BAEP is insensitive to anesthetics including volatile agents. Therefore, the change, if it occurs, cannot be attributed to the anesthesia. Wave V latency prolongation greater than 1 ms and amplitude depression greater than 50% are empirically regarded as alarming criteria (see Fig. 7-16).

## **ELECTOCORTICOGRAPHY (ECoG) AND INTRACRANIAL RECORDING**

### **ELECTROCORTICOGRAPHY**

ECoG is used for surgical procedures to determine the epileptogenic zone, that is, localization of spike or spike-and-wave discharges recorded directly from the cortex.

The technologist is responsible for creating a quality recording in an electrically hostile environment. Because the electrode impedance tends to be higher than conventional disc electrodes and electrode placement is unstable, slight movements in the surgical field or movement of personnel around the bed or touching the input cable may cause a variety of artifacts. Some of these artifacts resemble genuine EEG activity

and thus various activities in the operating room must be correlated and documented in relationship to the EEG pattern. All electrical equipment not used for the procedure should be removed or powered off to avoid the contamination of 60 Hz or other artifact. If artifact is still being recorded, make sure that all cables are connected properly and ask surgeon if all cortical electrodes are placed securely and making contact with the cortex.

The electrodes used for ECoG come in sterile packaging and are composed of small contacts set in a silicone base. The number of contacts to be used varies depending on the surface area to be covered (see Fig. 9-2). The surgeon will hand the electrode wires to the technologist to be plugged into the electrode junction box that is outside the surgical field. This must be done with extreme care to ensure the location of the discharges are identified properly. Care must also be taken not to contaminate the surgical field.

Because the EEG recorded directly from the cortex is five to ten times larger in amplitude than scalp-recorded EEG, the sensitivity can be decreased. The reference is placed over the cortex, away from the active electrodes in the subgaleal space. Because the primary interest of electrocorticography is spikes and not slow waves, the low-frequency filter can be raised to 5 to 10 Hz, which may be useful in eliminating slow-frequency artifacts or interference patterns.

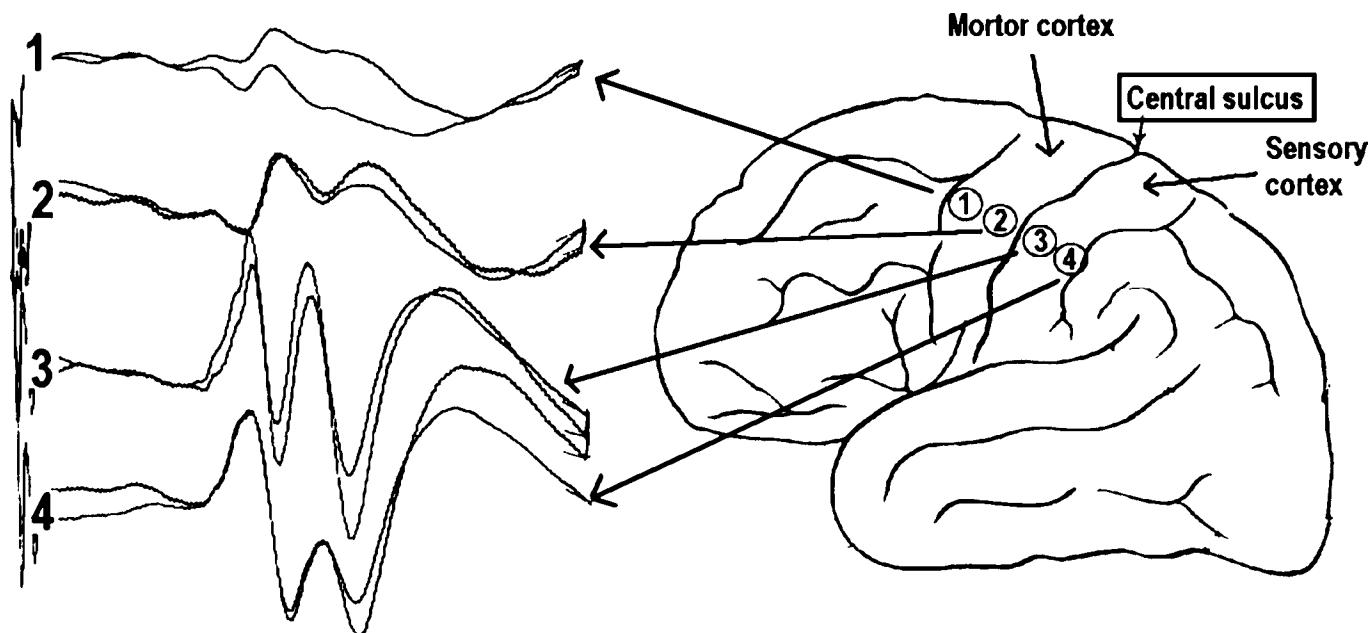
### **CORTICAL SOMATOSENSORY EVOKED POTENTIAL**

Another form of intracranial recording is the use of SSEPs for identification of the sensory and/or motor cortex. The study is often requested when a brain tumor or a lesion to be operated on is located in the frontal or the parietal lobe near the primary sensory or motor cortex. The neurosurgeon will use this information to avoid damaging eloquent tissue during removal of the lesion. The cortical potential is evoked after contralateral median nerve stimulation. A strip electrode of four to eight contacts is used and placed over the estimated sensory/motor cortex in an anterior-posterior longitudinal plane. Cortical SSEP shows a phase reversal across the central sulcus (Rolandic fissure). Therefore, identification of the motor or sensory cortex is a matter of finding the site where the SSEP shows phase reversal. The location of the electrodes should be estimated nearby the hand motor/sensory cortex. This is done by adjusting the location of the strip of electrodes until the phase reversal is identified (Fig. 5-5). Because the cortically recorded SSEP is much larger than scalp-recorded SSEP, usually 100 or fewer averaged responses are needed to acquire an adequate recording.

This type of recording has similar pitfalls and artifact contamination as encountered in the ECoG. It is the responsibility of the technologist to recognize and eliminate artifact.

## **TROUBLESHOOTING IN THE OPERATING ROOM**

Regardless of the modality being used, the operating room is an electrically hostile environment for neurophysiologic recording. One of the most valuable skills of a technologist is to be able to identify and eliminate sources of artifact. One of the



**Figure 5-5.** SSEPs recorded from the cortex overlying the sensory and motor cortices after stimulation of the median nerve. Note phase reversal of waveform across the central sulcus, which aids identification of motor and sensory cortices.

major sources of artifact is electrocautery. The electrical noise that is introduced by the cautery appears as very high voltage and is fast in frequency and cannot be entirely filtered out by changing the filter settings. This can easily distort or eliminate normal responses. If evaluation of the response is necessary during a critical phase of the surgery and the surgeon is using cautery, ask the surgeon to temporarily stop using the cautery. Thankfully, cautery is predominantly used during the opening/exposure of the surgical site and should not interfere much during the critical portions of the case such as during instrumentation. Even when cautery is not being used, it is best to keep the cauterizing instrument as isolated from the recording electrodes as possible since it can give off 60-cycle interference even when not in use.

In all OR cases, patients will be in contact with several pieces of equipment other than the neuromonitoring equipment. Some other common sources of interference are drills, fluid warmers, fluoroscopy and x-ray equipment, the anesthesia machine, body warmers, and microscopes. The use of this equipment is inevitable during surgery. The best thing to do is document when they are being used in order to correlate artifact with the use. Avoid using the same outlet with the instruments causing artifacts.

In order to eliminate artifact, the technologist must first be able to discern artifact from physiologic responses. The technologist is not responsible for the interpretation of data but should be well educated on the modalities they are using, so they can recognize wave forms specific to that modality.

The equipment being used in the monitoring of neurophysiologic data can frequently be the source of recording problems. Loose cables and improperly secured electrodes (recording or stimulating) are common causes of stimulus artifact. Electrodes should be well secured to the patient to ensure low impedance. Electrode cables should also be bundled together

as this reduces the risk of them being pulled out and will also help reduce the 60 Hz or other interference activity. It is very common for the input cable that connects to the junction box to be mishandled; it may get pulled and stepped on. If the cord is placed as out of the way as possible (try running them under the bed frame), it will decrease the likelihood of getting pulled out. Equipment well maintained by a biomedical engineer will help prevent problems from occurring during monitoring.

A useful tool available on most monitoring equipment is the ability to view or monitor the “live input data.” This allows evaluating the pattern, frequency, and amplitude of artifacts. This may help find the source of interference. If there is large 60-Hz interference; try separating your power/amplifier cables from the power supply of other equipment. Separating cords may seem like a trivial detail, but it can make a significant difference in the quality of recording. The use of 60-Hz filtering is prohibited in evoked potential recording, because its use will cause 60-Hz ringing that may mimic the response (see Fig. 1-14) and/or eliminate or distort the response. If 60-Hz filtering has to be used, one should be keenly aware of the above pitfalls. If the interfering artifact has fixed frequency, changing the stimulus rate slightly may help to minimize the artifacts by “averaging out” the artifacts.

Not all troubleshooting in the operating room involves mechanical or electrical systems. Other factors that can affect the ability to elicit responses must be considered. The primary nonelectrical issue that must be faced in the OR is the effect of anesthesia. If the levels of anesthetics are such that responses would be unobtainable, this must be documented and addressed. The other nonelectrical/mechanical factors involved in troubleshooting are the patient’s vital signs and positioning. If the patient’s vitals, such as blood pressure and temperature, are too far out of the normal range, responses may become increasingly difficult to obtain. Positioning of the arm and leg is

also important, and care must be taken not to hyperextend joints or compress vulnerable nerves in a prolonged and fixed position. A small adjustment to the body or limb position will often quickly reverse the altered response.

Following is an example of a checklist for troubleshooting, though different facilities may encounter different problems and modifications may be needed depending on the facility.

- Are baseline (control) responses stable and reproducible?
- Are anesthetics appropriate for the modality being recorded?
- Are all electrodes secured and bundled together with low impedances including ground and stimulus electrodes?
- Is stimulus intensity sufficient?
- Are all cables connecting patient to recording equipment plugged in and securely and correctly connected?
- Are recording equipment cables and electrodes as isolated from other equipment as possible?
- Is all unnecessary equipment disconnected from power supply?
- Is patient positioned in a manner that avoids compression of the nerves?
- Are patient's vital signs (blood pressure, temperature, respiration, etc.) in adequate range?

## THE EFFECT OF ANESTHESIA

While it is important to keep the patient asleep during surgery, it is also important not to overanesthetize the patient, which could eliminate all responses the technologist is trying to acquire. The balancing of the two is often a fine line. The benefit of anesthesia for NIOM is that higher-stimulus intensity can be used because the patient is anesthetized and that the responses are often better defined and "cleaner" than those obtained while the patient is awake. However, anesthesia has a dramatic effect on waveforms; therefore, the response under anesthesia could be quite different from that obtained while the patient is awake. The longer latency or polysynaptic components are more sensitive to anesthetics than short latency or oligosynaptic potentials. For example, P14 and N20 (subcortical and first cortical potentials, respectively) are less affected by anesthetics than the subsequent components (P26-N30-P40-N60).<sup>4,11</sup> All halogenated inhalation agents tend to attenuate or abolish evoked potentials and prolong the latencies. TcMEPs are far more sensitive to anesthesia than SSEPs.<sup>12</sup>

## INHALATION ANESTHETICS

The common halogenated agents are nitrous oxide ( $N_2O$ ), halothane, desflurane, isoflurane, etc. The relative potency of the inhaled agent is described by the MAC (minimal alveoli concentration) value, where one MAC is defined as preventing movement to painful or surgical stimuli in 50% of patients. The actual concentration needed to obtain one MAC value varies among anesthetic agents, for example, one MAC for isoflurane is 1.3%, but for halothane it is 0.7%. The short latency responses (brainstem components, far-field potentials) are more resistant than long latency responses (cortical components). Thus, short latency far-field potentials of P14 and P31, for upper and lower extremity SSEP, respectively, are useful markers under inhalation anesthesia.<sup>4</sup> Generally, it is possible to obtain consistent

and well-defined far-field SSEPs with isoflurane greater than 1% with 50% to 60%  $N_2O$ . However, TcMEPs usually cannot be recorded with isoflurane greater than 0.5%.

## TOTAL INTRAVENOUS ANESTHESIA (TIVA)

More recently, TIVA has become increasing popular for neurophysiologic monitoring. TIVA includes barbiturates, opioid (morphine, alfentanil, sufentanil, remifentanil, etc.), propofol, etomidate, and ketamine. Barbiturates are often used for induction of general anesthesia and have similar effect on evoked potentials as that of halogenated agents. Propofol is beneficial because of its short duration of action and minimal effect on SSEPs and TcMEPs. Both ketamine and etomidates are called EP "friendly" agents and may even enhance the response by heightening of synaptic function at low dose.

## MUSCLE RELAXANT

Muscle relaxants (pancuronium bromide, vecuronium bromide, atracurium) are often used with combinations of intravenous or inhalation agents. The so-called balanced anesthesia includes narcotics for analgesia plus a muscle relaxant with a relatively weak anesthesia such as  $N_2O$ .<sup>11,12</sup>

The muscle relaxant does not negatively affect SSEP and has the benefit of eliminating muscle artifacts, but it abolishes muscle potentials associated with stimulus delivery to a mixed nerve; therefore, it may give the erroneous impression that adequate stimulus is not being delivered. The technologist should document the degree of paralysis if a muscle relaxant is used. The use of a muscle relaxant is detrimental for MEP recording. It is our experience that MEP cannot be reliably recorded if there are fewer than two twitches of four repetitive stimulations on a "twitch monitor." If the patient is totally paralyzed, alternative methods such as a spinal cord recording (I and D waves) after transcranial electric stimulation may be considered (see Fig. 7-9).

## PATIENT SAFETY

One of the most important responsibilities for the NIOM specialist is patient safety. Throughout preparation and monitoring of the responses, certain patient safety issues can be overlooked or forgotten. Statistics show that 4 in 1,000 patients (in the United States) per year sustain some type of burn from consumer products, which adds up to about 300,000 burns per year; 3% of these are electrical burns.<sup>13</sup> There are four types of burns that can occur: mechanical, chemical, electrical, and electrochemical injuries.<sup>13,14</sup> Mechanical injury can occur during the process of preparing the skin for surface electrodes. An overzealous technologist can easily remove superficial layers of skin by simply rubbing too hard in order to bring down impedances. The technologist needs to be aware of the patient's skin condition and how fragile it might be, especially with elderly patients. The technologist should also be careful when removing the electrodes and adhesive to minimize injury to the skin at the end of the procedure.

Mechanical injury can also be caused by prolonged direct pressure. In some lengthy cases, the patient stays in the same position for a long time. Nerve or vascular compression can not

only result in pain after surgery is over but can also result in a loss of peripheral action potential. When peripheral potential of one limb is lost during monitoring without specific reason, consider nerve compression or ischemia due to unusual posture or limb position. Slight adjustment of limb position may recover the lost peripheral nerve potential.

Chemical burns or injuries are caused by a toxic chemical on the surface of the skin. The patient's chance of this type of injury increases after the minor trauma of skin preparation during the process of electrode application. This is more likely in children than adults. Other things that can produce chemical burns are the conductive gels or paste and the electrodes themselves. Metal electrodes composed of nickel and stainless steel may cause dermatitis if the patient is allergic to it.

Electrical burns can be caused by four different mechanisms: local heating (produced by current passing through resistant material), electroporation (direct effect of the electrical field produced by electrodes on cellular membranes), electroconformational denaturation (cellular protein damage), and overstimulation of neural tissues (possible with direct stimulation of the cortex). To prevent burns in the operating room, be sure to check the equipment, and make sure it has been inspected and tested by the biomedical department. Look at the electrosurgical equipment and check for biomedical inspection dates. Check all the cables from your equipment (recording and stimulating), making sure insulations are intact. Inspect the electro-surgical grounding pad. Make sure it is not too close to your recording or stimulating electrodes and is securely in place.

Always be aware of what is occurring in the operating room suite. Make sure all cables, stimulus boxes, and recording amplifiers are dry and out of the way of other equipment. Do not bundle electrode wires with other cables, especially from other equipment.

Part of patient safety is also the technologist's personal safety. Be careful when removing needle electrodes to make sure you do not stick yourself. Disposable needles should be discarded in approved sharp containers. Be courteous to the operating room staff by alerting them to the location of needles, so they are not accidentally stuck by a soiled needle. Most importantly, communicate with the surgeon and the anesthesiologist especially when there is a potential problem.

In conclusion, NIOM is a complex process and takes a dedicated and organized team to coordinate all the steps involved from the preoperative phase to recovery. In addition to the surgical staff, having a technologist with diverse knowledge of surgical procedures and the modalities used to protect the patient during those procedures is necessary. They must also have critical thinking skills and the ability to perform in a high-stress environment. Education and experience are a must to be successful in NIOM.

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# EEG Monitoring for Carotid Endarterectomy

## INTRODUCTION

The studies from the North American Symptomatic Carotid Endarterectomy Trial Collaborators<sup>1</sup> have shown the benefit of carotid endarterectomy (CEA) in preventing stroke, especially for patients with high-grade carotid artery stenosis.

CEA can be performed under either general or regional (local) anesthesia. During CEA, the internal carotid artery must be cross-clamped (clamped above and below the area of concern); therefore, the brain becomes subject to ischemia or hypoperfusion. The brain can tolerate decreased blood flow for more than 1 hour if cerebral blood flow is greater than 15 mL/100 g/min, but a total lack of blood flow would result in a severe infarction within 4 minutes. The brain can sometimes tolerate a complete loss of cerebral blood flow from one carotid artery following cross-clamping if there is adequate collateral circulation from the opposite carotid artery via the circle of Willis or from the vertebrobasilar artery (see *Practical Guide: EEG*, Chapter 5, Figs. 5-10 and 5-11). Whether a shunt is required (to bypass the cross-clamped area of the carotid artery) or not is dependent on the degree of the collateral flow. A number of monitoring techniques are available for examining cerebral perfusion and detecting the risk of cerebral ischemia after cross-clamping the artery. These include EEG, somatosensory evoked potentials (SSEPs; median nerve stimulation), transcranial Doppler (TCD), and oxygen saturation of hemoglobin using near-infrared spectroscopy.

Because the placement of the shunt itself carries a significant risk of embolization as a result of dislodging atherosclerotic emboli coming from the vessel wall, only patients with a potentially high risk of developing ischemic brain damage are selected for shunt placement. Determining which patients require shunts depends on multiple factors. EEG has been the most commonly used monitoring method for determining the need for a shunt, but other tests are complementary or may be more sensitive and accurate for predicting ischemic insult.

## ANESTHESIA

Most CEAs are performed under general anesthesia. A commonly used anesthesia for CEA surgery is gaseous anesthesia with

isoflurane ranging between 0.4% and 0.6% with 40% to 60% N<sub>2</sub>O and oxygen. This combination may be supplemented by sufentanil or remifentanil.<sup>2,3</sup> An alternative anesthetic regimen consists of nitrous oxide in oxygen and propofol after induction with etomidate and fentanyl.<sup>3</sup> Other commonly used inhalation agents include desflurane, enflurane, and sevoflurane.

### EEG CHANGES DURING INDUCTION

Most anesthesia inductions are carried out by etomidate, propofol, or thiopental via intravenous administration. This initially produces an EEG showing beta activity with a decrease in the alpha rhythm. The beta activity rapidly becomes more widespread, with increases in amplitude. This is followed by a slowing in the beta frequency that approaches the alpha frequency. During this phase, the beta or alpha activity may be intermixed with a burst of high-amplitude, intermittent rhythmic delta activity, which is often of frontal dominance, that is, FIRDA (frontal intermittent delta activity) before a steady-state anesthetic pattern is established (Figs. 6-1A and B and 6-2A and B).<sup>4</sup>

### EEG PATTERNS AT SUB-MAC CONCENTRATION

Most CEAs are done under sub-MAC concentration. MAC (mean alveolar concentration) is defined as the percentage of inhaled gas at which 50% of patients will not move after abdominal incision. At this light level of steady-state anesthesia, a widespread, anteriorly dominant rhythm (WAR) pattern, usually in the lower beta or alpha frequency activity is seen with all of the above-described agents.<sup>4</sup> The frequency of this pattern tends to slow with increasing concentration of these agents. This anesthetic WAR pattern is strikingly similar to the alpha coma pattern often seen in a postanoxic cerebral insult (Figs. 6-1D, 6-2D, 6-3A, and 6-4A).

### EEG PATTERNS DURING RECOVERY FROM ANESTHESIA

When discontinuing anesthetics at the sub-MAC level, the WAR pattern decreases in amplitude and increases in frequency, which subsequently changes to beta range activity. During the transition from the anesthetic state to the arousal state, bursts of intermittent delta activity resembling a FIRDA pattern may

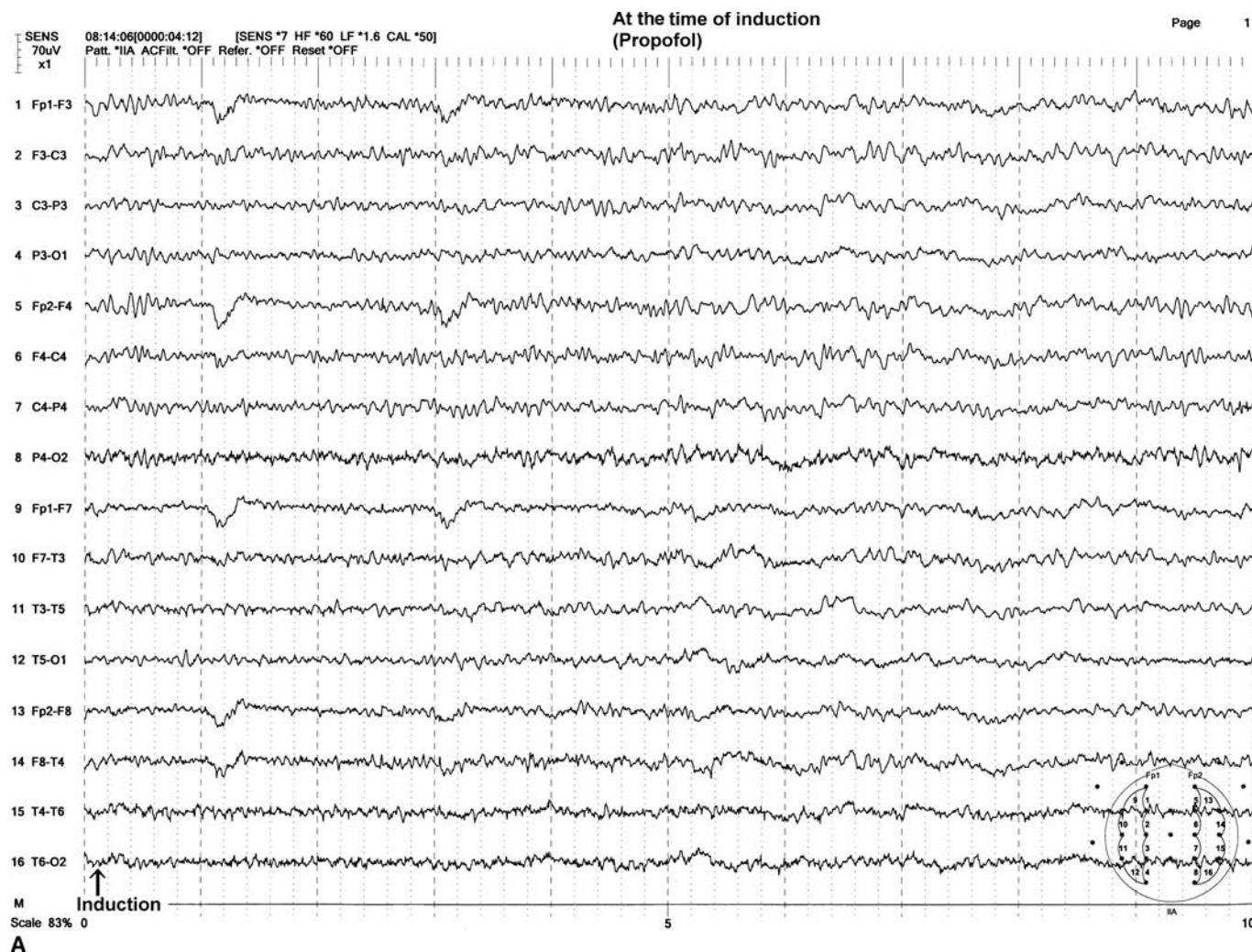
appear that are similar to but less prominent than those seen during induction.

#### OTHER FACTORS THAT AFFECT EEG

Decreasing the  $\text{PaCO}_2$  (arterial pressure) level below 40 mm Hg or decreasing the amount of stimulation that would be painful if given during the awake state would produce a pattern suggestive of a deeper level of anesthesia, that is, increase of slow waves. A severe blood pressure drop is associated with an increase of slow waves and an eventual flattening of the EEG activity. Hypothermia also slows the EEG frequency spectrum with gradual reduction of amplitude, eventually leading to EEG “flattening” at about 20 to 25°C. However, electrocerebral inactivity created by severe hypothermia can be reversible and perhaps acts as a cerebral protective mechanism.

## EEG MONITORING

EEG has been used for monitoring brain function during CEA for many years and probably has been the most commonly used method for detection of cerebral ischemia that would determine the need for selective shunting. EEG can be recorded easily in the operating room despite an electrically hostile environment where multiple electrical instruments are connected to or working nearby the patient and the surgical personnel. Most EEG monitoring is performed under general anesthesia, and its activity may vary depending on the type and depth of anesthesia, blood pressure, body temperature, or other physiological factors such as  $\text{PaCO}_2$  and  $\text{PaO}_2$  levels. These variables should be thoroughly understood by the monitoring team.



**Figure 6-1. A–D.** EEG examples of the anesthetic effect using isoflurane and nitrous oxide. The patient is a 50-year-old woman having a history of transient ischemic attack (TIA) symptoms with intermittent partial visual loss in the left eye with right extremity weakness. **A:** Within five seconds after IV propofol injection, the EEG starts to show diffuse delta with superimposed beta activity. (This patient had preexisting beta activity prior to induction). **B:** Subsequent polymorphic delta activity with superimposed beta activity is seen. This was followed by **C**, which shows a decrease of delta activity along with the widespread anteriorly dominant rhythm (WAR) consisting of dominant alpha and beta activities. In addition, there were occasional anterior dominant intermittent slow (AIS) and widespread (irregular) persistent slow (WPS) patterns. **D:** When the anesthesia was stabilized at sub-MAC level, AIS and WPS patterns became less frequent and less prominent, and WAR pattern dominated throughout the procedure (From Yamada and Yeh. Monitoring EEG during carotid surgery. In: Schomer D, da Silva FH, eds. *Niedermeyer's Electroencephalography*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2011, with permission.)



**Figure 6-1. Cont'd.**

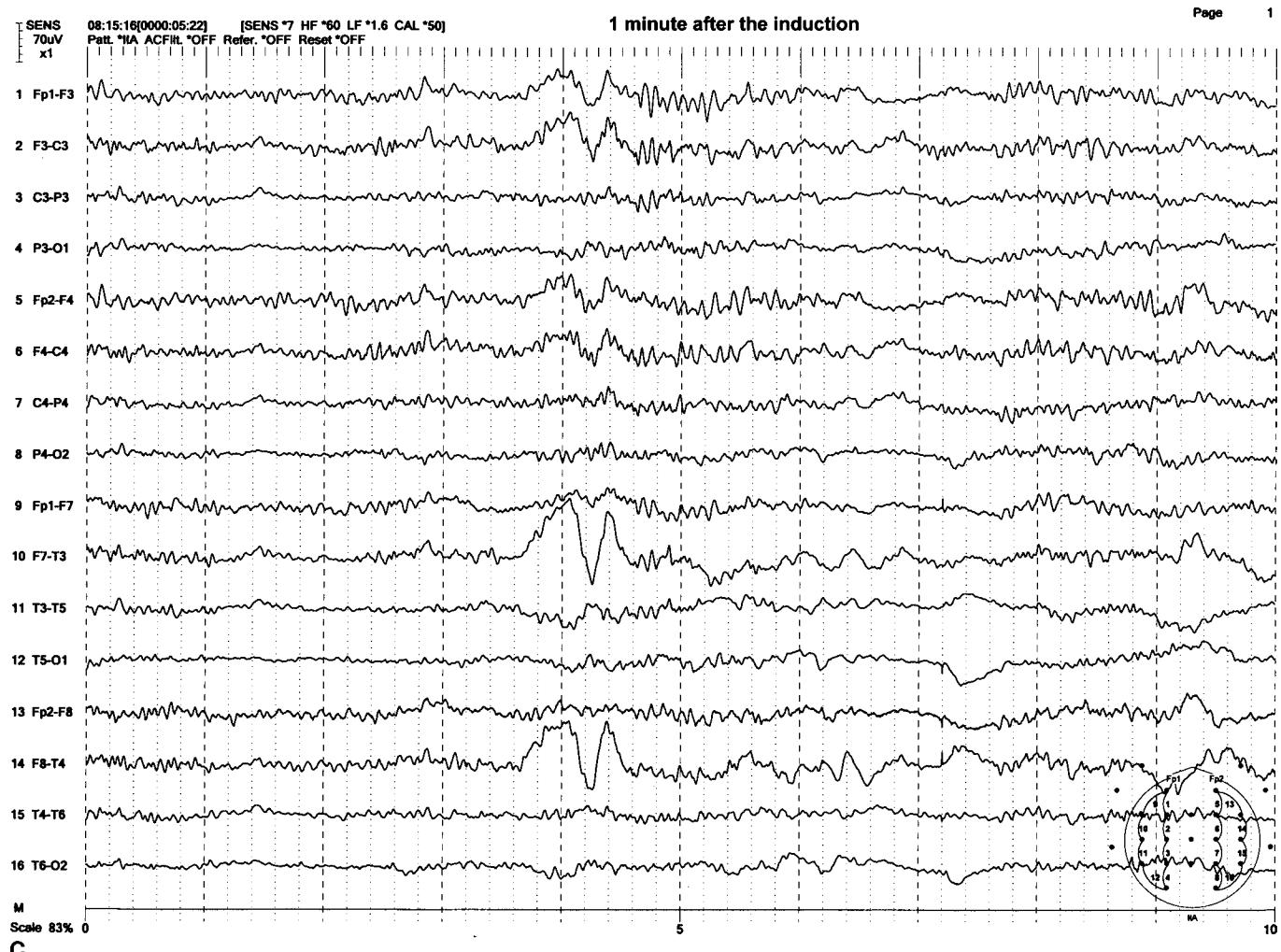
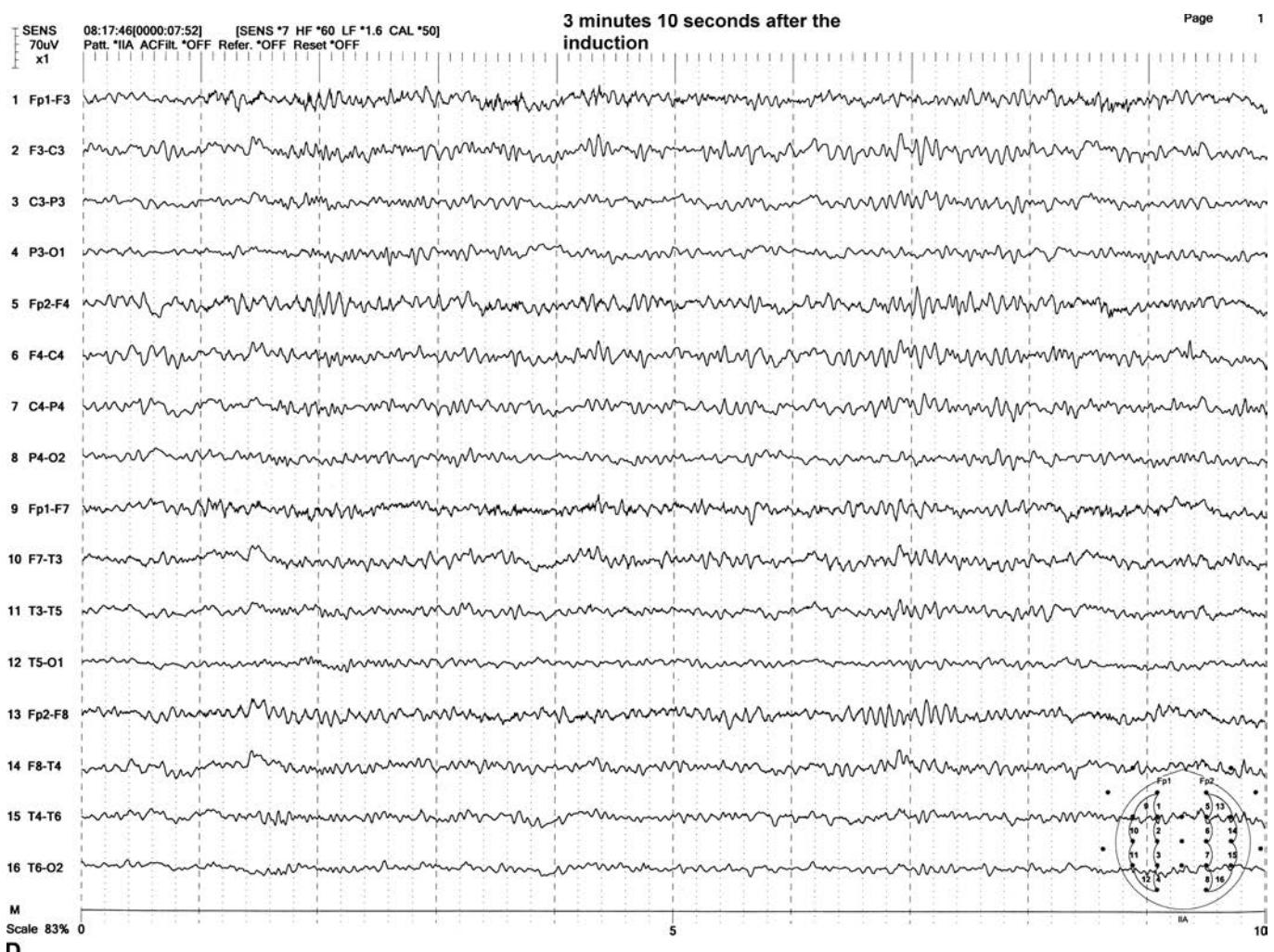
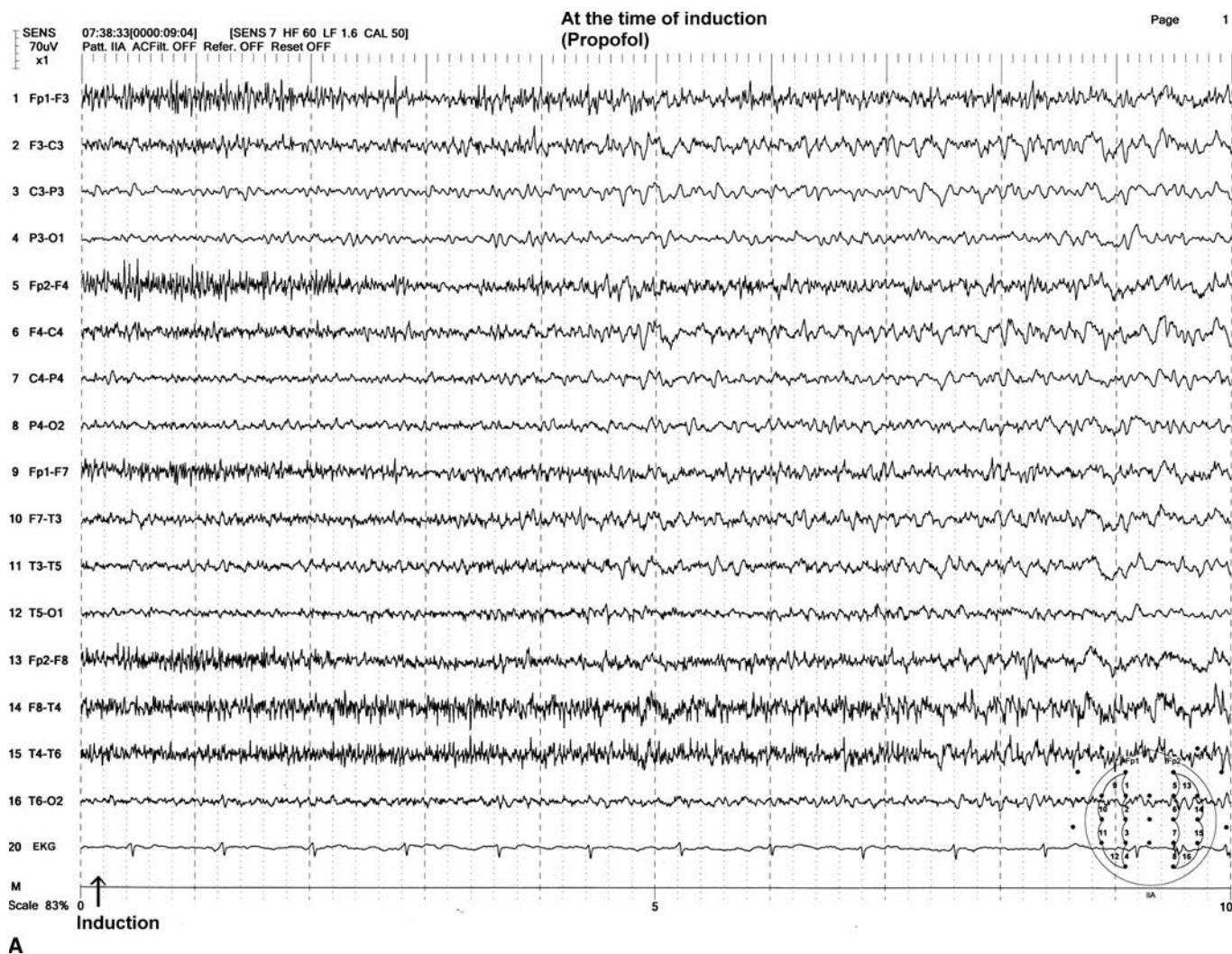


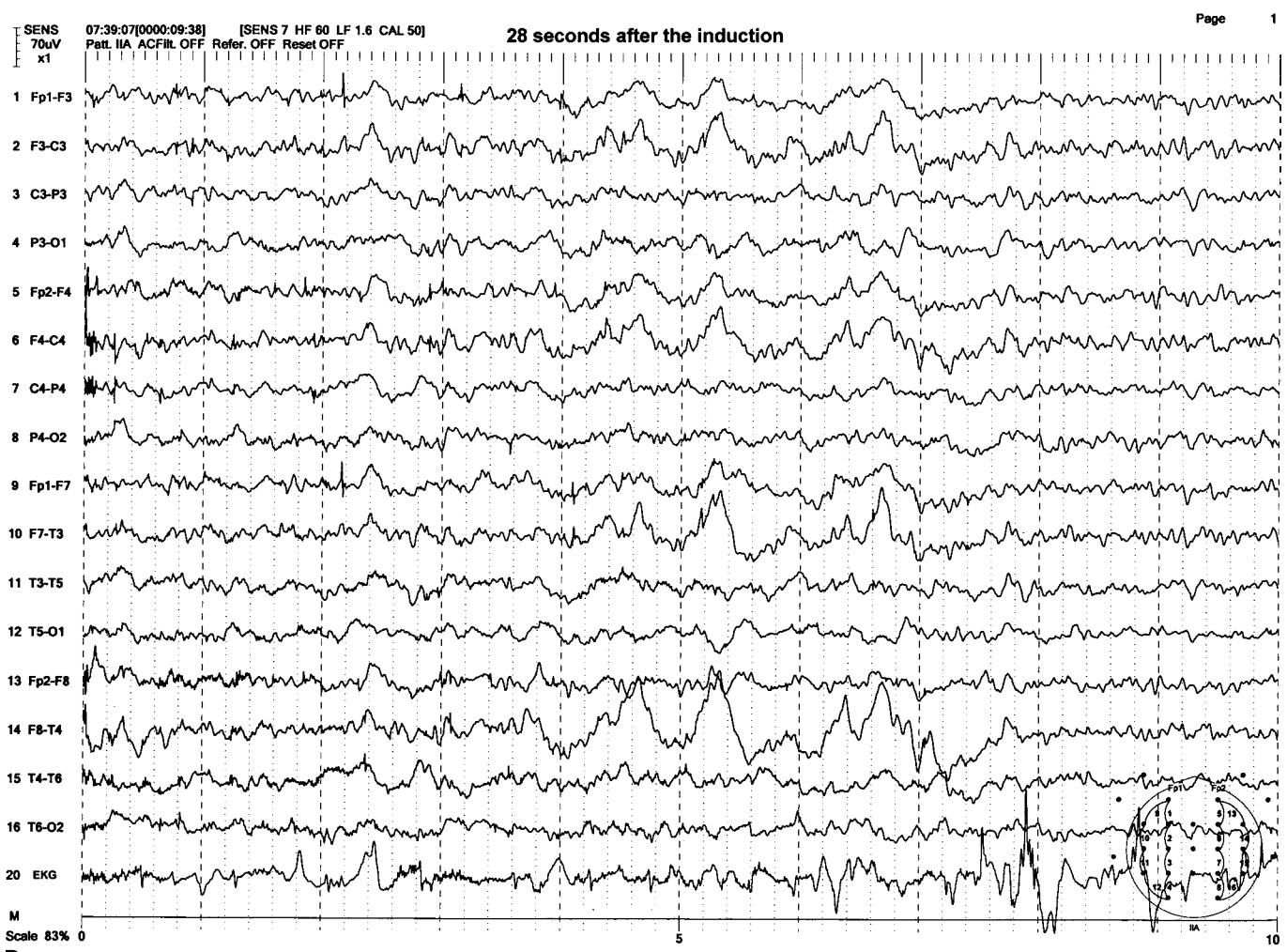
Figure 6-1. Cont'd.



**Figure 6-1. Cont'd.**



**Figure 6-2.** A–D. Another EEG example of anesthetic effect using desflurane and nitrous oxide. The EEG monitors a right CEA in a 66-year-old man without a history of TIA or stroke but having a 70% to 80% stenosis on right and 50% to 60% stenosis on left carotid artery. **A,B:** Within 5 seconds after the IV propofol injection, the EEG started to show diffuse theta activity mixed with beta activity, which was followed by an increase of irregular delta as well as frontal dominant rhythmic delta activity (FIRDA) within 30–40 seconds after the induction. **C:** About a minute after the induction, delta slow waves became more dominant with irregular delta (WPS) along with a frontal dominant intermittent delta (AIS) pattern. **D:** Once the anesthesia was stabilized at the sub-MAC level, the EEG was dominated by diffuse alpha and slow beta activity with minimal theta-delta components, resembling “alpha-coma” (From Yamada and Yeh. Monitoring EEG during carotid surgery. In: Schomer D, da Silva FH, eds. Niedermeyer's Electroencephalography. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2011, with permission.)



**Figure 6-2 Cont'd.**



C

**Figure 6-2. Cont'd.**

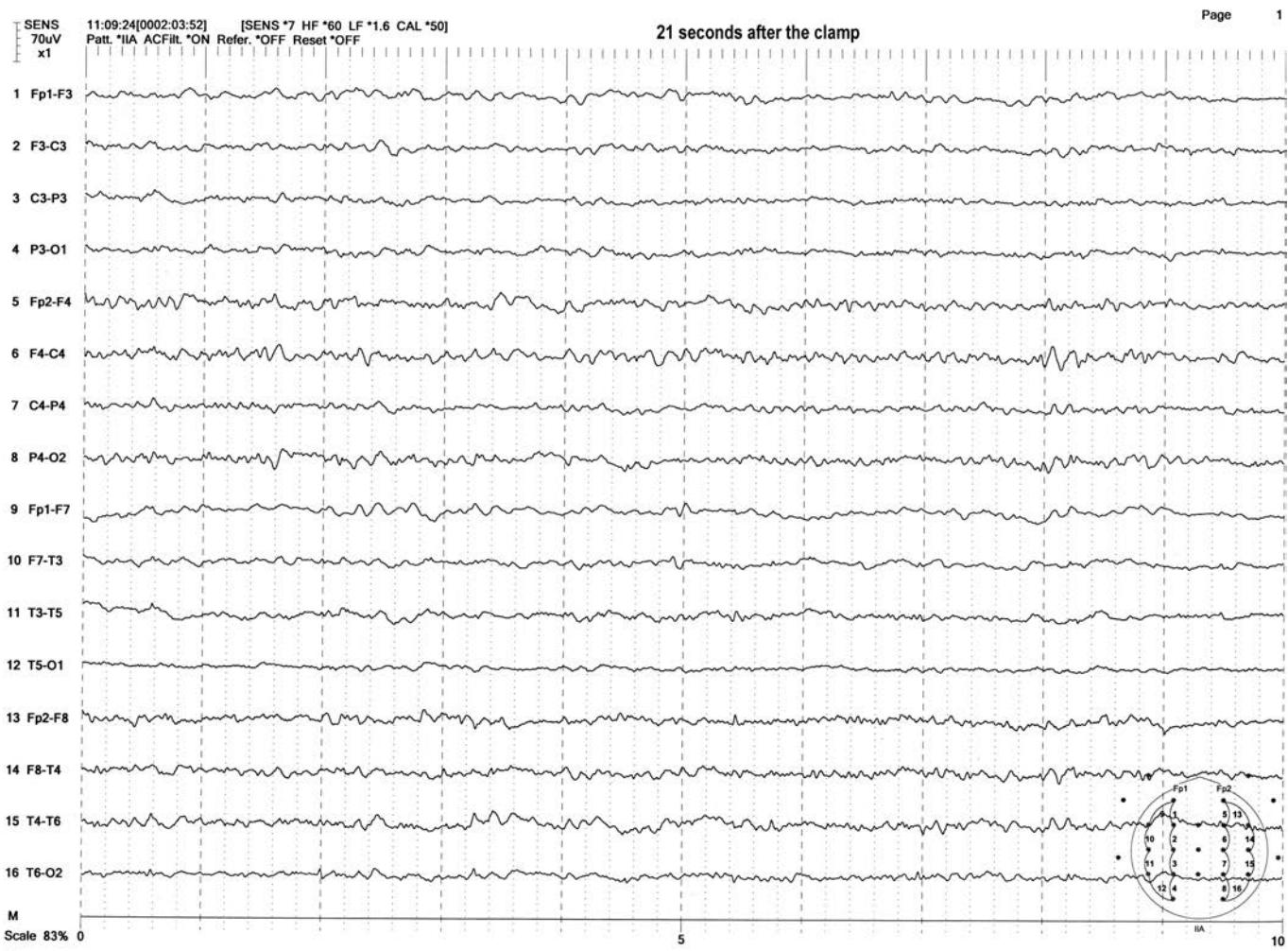


D

Figure 6-2. Cont'd.



**Figure 6-3. A–D.** A 69-year-old man without a history of TIA or stroke has a 90% stenosis of the left carotid and a patent right carotid artery. **A:** Within several seconds after cross-clamping the left carotid artery, there was a slight reduction and slowing of the alpha activity noted, more prominently in the left hemisphere. Note the dominant WAR pattern with alpha activity resembling an "alpha coma" prior to the clamp. **B:** The suppression of EEG activity in the left hemisphere became more prominent within 20 seconds after carotid clamp. This persisted until the shunt was placed. Within a few seconds after the shunt was placed, the EEG started to show recovery (C). It took more than 3 minutes to recover fully to the preclamp EEG (D). (From Yamada and Yeh. Monitoring EEG during carotid surgery. In: Schomer D, da Silva FH, eds. *Niedermeyer's Electroencephalography*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2011, with permission.)



B  
Figure 6.3. Cont'd.

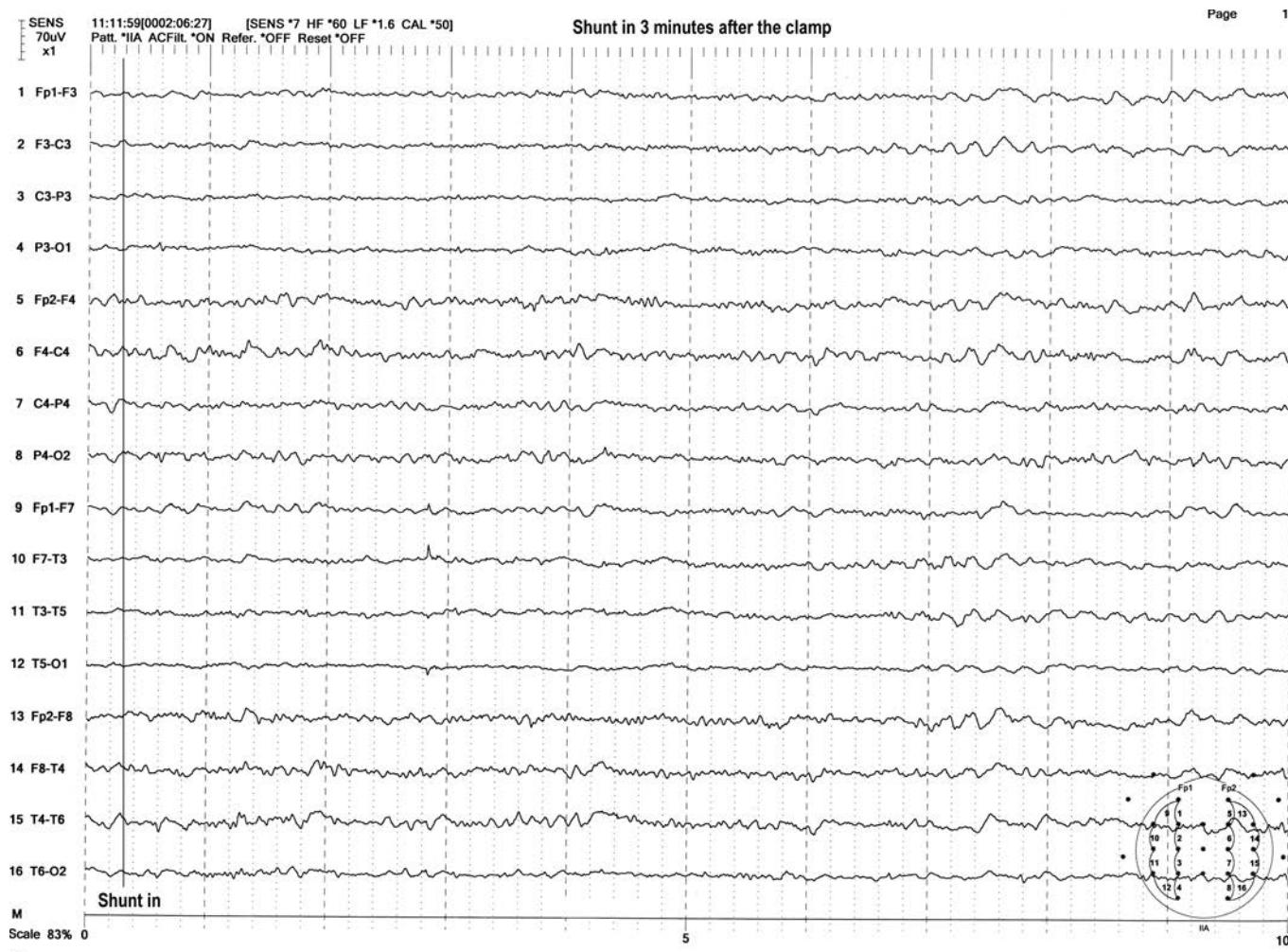


Figure 6-3. Cont'd.



Figure 6-3. Cont'd.



**Figure 6-4. A–D.** A 77-year-old man without a history of TIA or stroke has occlusion of right carotid and an 80% stenosis of left carotid artery. **A:** The EEG started to show an increase of theta and delta range activity bilaterally within 5 seconds after the clamp. **B:** Within 20 seconds after the clamp, the EEG showed diffuse suppression and loss of fast activity bilaterally that was to a greater degree over the left hemisphere (**B**). **C:** Within a few seconds after the shunt was placed, the EEG started to recover. **D:** Full recovery was achieved at about 1 minute after the shunt was placed (From Yamada and Yeh. Monitoring EEG during carotid surgery. In: Schomer D, da Silva FH, eds. *Niedermeyer's Electroencephalography*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2011, with permission.)

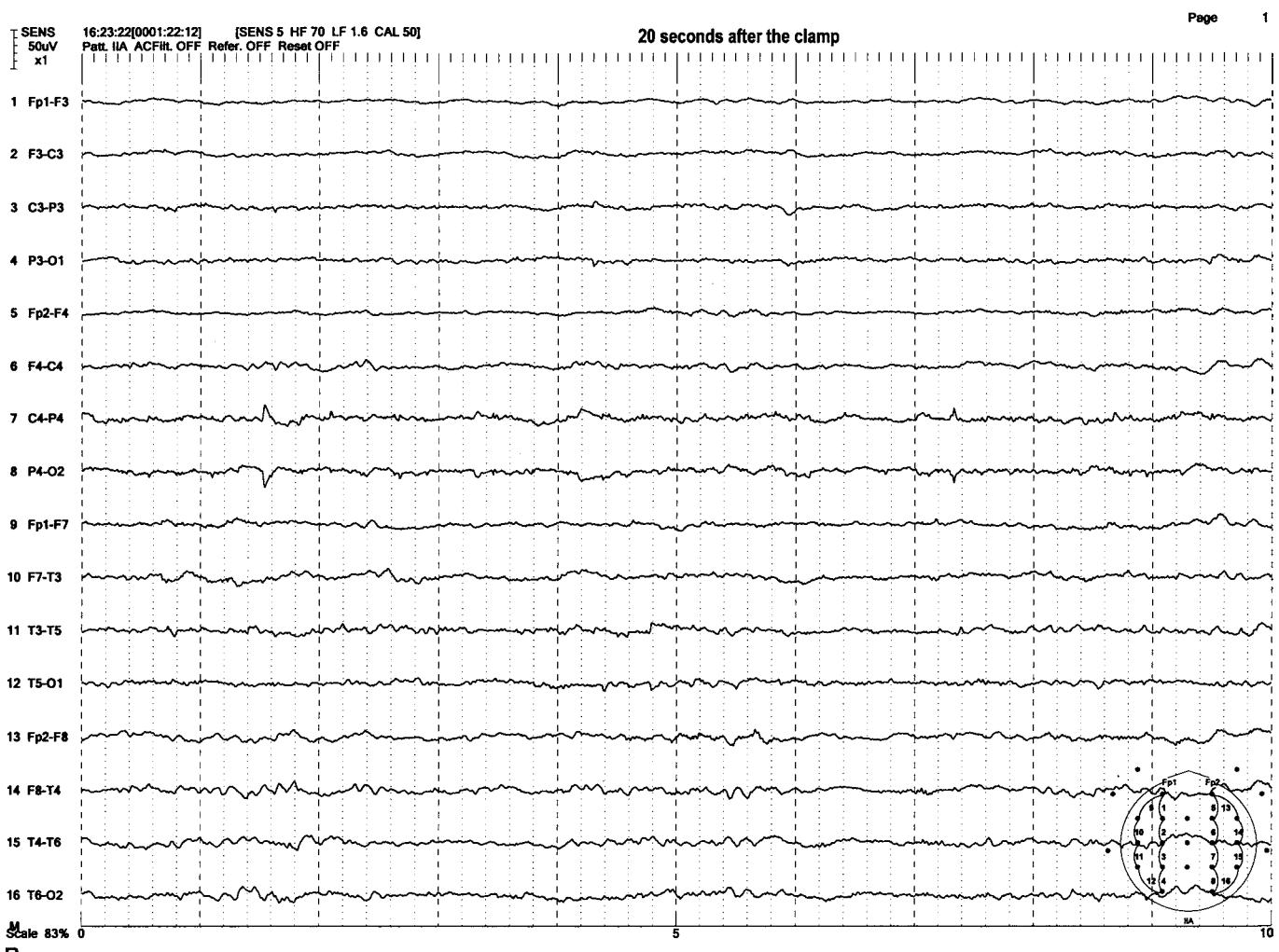


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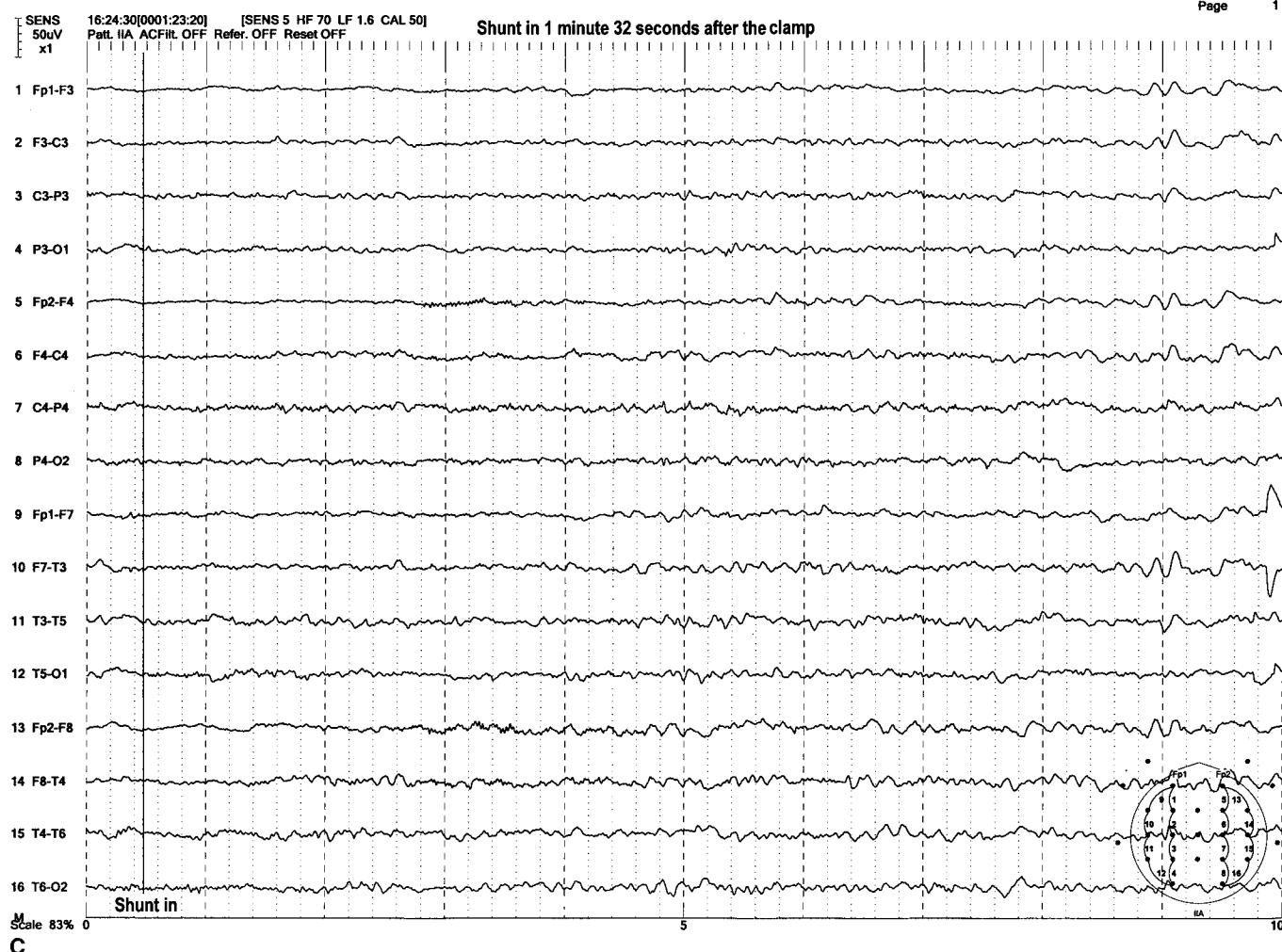


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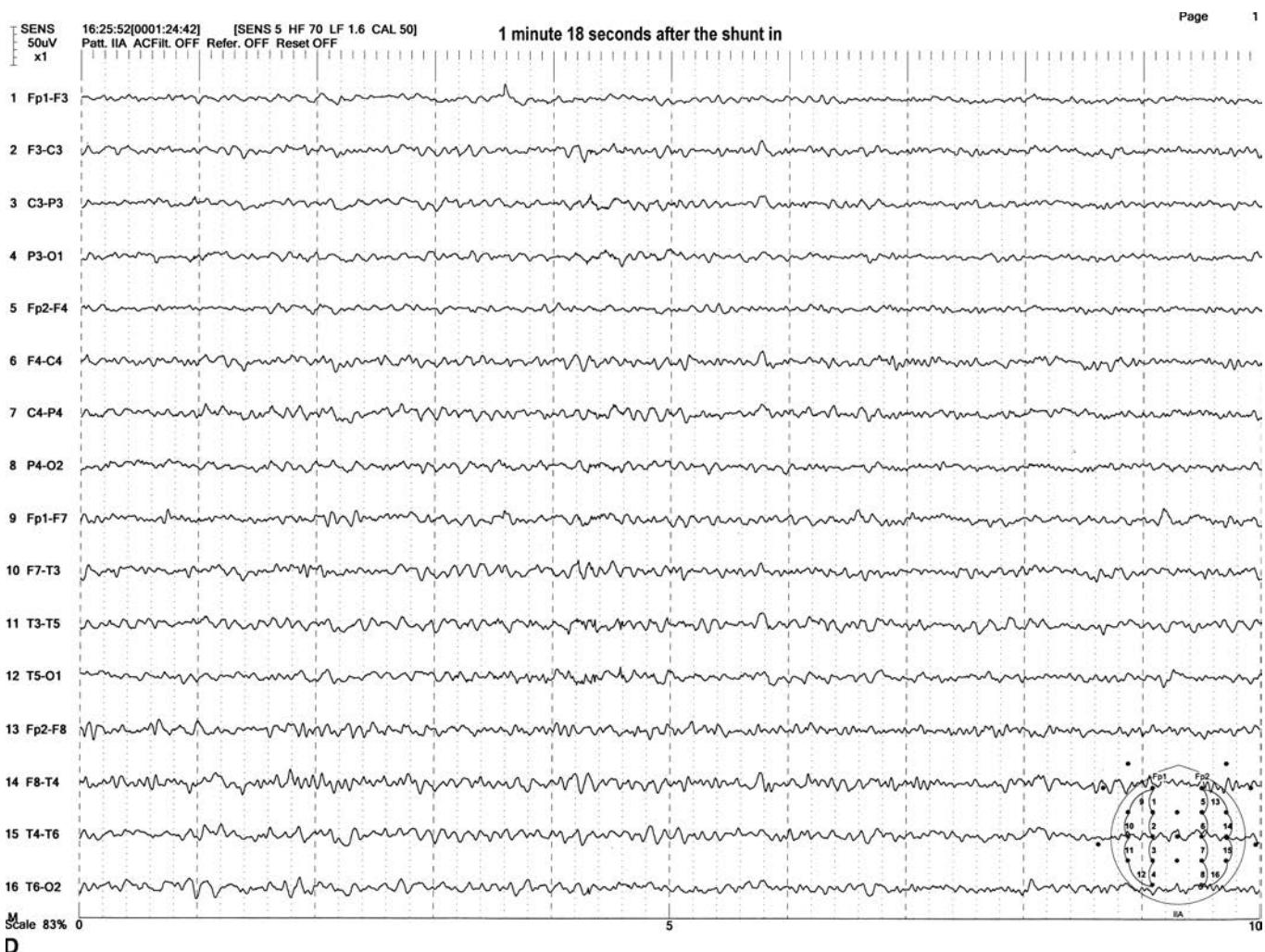


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## RECORDING TECHNIQUE

Because EEG changes during the CEA can be diffuse or focal, electrodes across the entire scalp, using 16 EEG data channels are commonly used. It is preferable to use collodion, which ensures the secure attachment of electrodes to the scalp during the surgery.

The anterior-posterior longitudinal bipolar (the so-called double banana) montage is commonly used because this montage allows easy detection of hemispheric asymmetry.

The filter setting is usually the same as for routine EEG with the high (low pass) filter of 35 to 70 Hz. and the low (high pass) filter of 0.3 to 1 Hz. Because of the electrically “noisy” operating room environment, 60-Hz contamination onto the EEG recording may be inevitable. The monitoring team should try to find the source of the 60-Hz artifact and eliminate the artifact using technical modifications if possible. If 60-Hz artifacts cannot be eliminated, the use of 60-Hz notch filter is allowed.

The sensitivity setting is usually 7 or 5  $\mu$ V/mm. It is not uncommon for the EEG amplitude to be exceedingly low under anesthesia, requiring a sensitivity of 3  $\mu$ V/mm.

The sweep speed is usually a 10-second display on a full video screen but may be adjusted to a 20–30 second screen that may make visualization of focal or hemispheric slow waves easier. These choices are dependent upon the interpretation need and preference of the electroencephalographer.

A preoperative, awake and resting EEG can be recorded in the operating room before anesthesia induction. This allows inspection of any preexisting EEG abnormalities before anesthesia. At least 5 to 10 minutes of baseline preclamp EEG while the patient is under stable anesthesia is essential to appreciate any clamp associated EEG changes. After the clamp is applied, the EEG of the preclamp state may be displayed on half of the video screen, so that the postclamp ongoing EEG can be directly compared with preclamp EEG. Although most clamp-related EEG changes occur within 20–30 seconds after the clamping, the EEG should be monitored throughout the procedure because EEG changes may occur in the middle of the procedure, long after the clamp has been applied. Possible causes for the late EEG changes include hypoperfusion secondary to a lowered blood pressure, embolism, or shunt malformation if a shunt is used.

## PRECLAMP FOCAL EEG ABNORMALITIES IN RELATIONSHIP TO ANESTHESIA

The majority of EEG patterns during CEA show a symmetric baseline pattern before the clamping of the carotid artery. However, depending on case selection, 30% to 40% of preclamp EEGs may show focal abnormalities of varying degrees.<sup>5</sup> The focal abnormality may consist of unilateral reduction of the WAR amplitude. This may be accompanied by polymorphic delta activity on the side of the reduced amplitude. Most focal EEG abnormalities under anesthesia correlate with preoperative waking EEG abnormalities. However, anesthesia may activate an abnormality that was either not apparent or less apparent during the waking state.<sup>4</sup> Conversely, anesthesia may obscure a focal abnormality in some cases that was apparent in EEG recordings during the wake state.

In patients with a lesion in the anterior head region where the alpha rhythm tends to be unaffected in the wake state, anesthesia may bring out a reduction of the WAR pattern along with

decreased beta and increased polymorphic slowing in the anterior head region. Preexisting intermittent rhythmic delta in the temporal region in the wake state may become more prominent and persistent, along with a reduction of the WAR pattern.<sup>4</sup> A more posterior lesion having decreased alpha activity on the side of the lesion may leave the anesthetic WAR pattern symmetrical without focal slowing.<sup>4</sup> Preexisting nonlateralizing FIRDA or persistent generalized slowing during the wake state may be observed and cannot be distinguished from the anesthesia-induced slowing that commonly occurs during induction or during the recovery phase of anesthesia.<sup>4</sup>

## EEG CHANGES AFTER CROSS-CLAMPING THE CAROTID ARTERY

Most preclamp EEGs have a symmetrical pattern without focal features, and the development of an asymmetric pattern after the clamp can be easily recognized. The clamp-associated EEG change occurs within the 1st minute in the majority of patients (>80%), with most (69%) appearing within 20 seconds after the clamp.<sup>6</sup> The most common and sensitive EEG change indicating cerebral ischemia is the decrease of alpha and beta frequency activity (WAR pattern) on the clamped side (Figs. 6-3A and B and 6-4A and B). Some laboratories use intravenous administration of benzodiazepine in order to induce beta activity onto the EEG, therefore making its reduction after clamping more readily visible. Fortunately, the most common EEG pattern under stable sub-MAC level of anesthesia consists of abundant alpha and beta activity (WAR pattern).

Further progression of ischemia is associated with an increase of delta amplitude or slower frequencies. The most severe degree of EEG change is “flattening” of the EEG pattern with depression of all activity including delta and faster frequency components (Figs. 6-3C and 6-4C). These changes occur primarily on the hemisphere ipsilateral to the side of clamp, but a bilateral change could occur if the blood flow of the contralateral hemisphere depends on the collateral circulation from the ipsilateral hemisphere. This may occur when occlusion or severe stenosis of the contralateral carotid artery exists. When bilateral changes occur, it may be difficult to differentiate if changes are due to global ischemia or systemic factors such as a change in anesthetic level, blood pressure, temperature, or  $\text{PaCO}_2/\text{O}_2$  level. However, the bilateral change secondary to hypoperfusion usually shows a greater EEG change where more “flattening” of EEG activity occurs in the presence of slower delta and/or greater depression of fast activity over the ipsilateral hemisphere (Fig. 6-4B).

After the shunt is placed, the EEG recovers gradually to the baseline state (preclamp EEG) and may take several minutes to fully recover. It appears that the longer the clamp time before shunt placement occurs, the slower the recovery time. In a small number of patients, the EEG improves but never recovers to the pre-clamp state. Most of these patients wake up with no neurological deficit, or if any, the deficit is minor or transient.

In the majority of shunted and nonshunted cases, the EEG remains symmetric throughout the procedure. In a small percentage of patients, transient and focal EEG changes may appear during the middle of the procedure, long after the cross-clamping has occurred. These transient and focal EEG

changes have been thought to be due to the asymmetrical effects of changing level of anesthesia or resurgence of preexisting focal abnormality. These transient changes usually have no neurological consequence.<sup>7</sup> This finding may be due to decreased blood pressure. Because the threshold of blood pressure to maintain adequate cerebral perfusion is not known and varies individually, slight reductions of systemic blood pressure may result in focal areas of ischemia bringing out EEG changes, especially when the blood pressure at the time of clamp is close to the threshold level. Raising the blood pressure usually corrects this adverse EEG change. Another possibility of late and persistent EEG change may be due to embolization, especially during dissection or at the time of clamp release that will likely result in neurological deficit.

A late EEG change may also occur in the shunted patient. If this is not due to blood pressure, anesthesia change, or embolization, a shunt malfunction should be considered.

### PREDICTABILITY OF EEG CHANGE

The overall incidence of clamp-related EEG changes has been estimated to be about 10% to 30%.<sup>5-8</sup> Most studies have agreed that the incidence of clamp-related EEG changes is higher in patients when the contralateral carotid artery was occluded. When patients with a patent and occluded contralateral carotid artery are compared, the patients with an occluded contralateral artery expectedly show greater incidence (~40%–50%) of EEG changes as compared with that (~10%–20%) of patients with a patent contralateral carotid artery.<sup>9-12</sup>

Clamp-related EEG changes are also more common in patients when contralateral abnormalities on the preoperative awake EEG exist than in patients with only ipsilateral or diffuse abnormalities<sup>6</sup> or patients with a previous history of stroke.<sup>13</sup> It should be noted that there are still a substantial number of patients who have a complete occlusion of the contralateral carotid artery who do not show EEG changes when clamping the ipsilateral carotid artery. This is likely due to adequate collateral circulation from the posterior cerebral artery. In such cases, the surgeon may prefer to shunt even if there is no EEG change since EEG does not reflect ischemia of small and deep regions such as the internal capsular region.

It is intuitive to expect that a greater degree of ipsilateral stenosis is associated with a lower chance of EEG change, because the collateral flow from the contralateral hemisphere would be better established in patients with severe stenosis than in patients with a patent ipsilateral carotid artery. However, one study did not support this expectation.<sup>14</sup>

### REGIONAL ANESTHESIA FOR AWAKE CEA AND EEG CORRELATES

The advantage of regional anesthesia (RA) instead of general anesthesia is that the patient's neurological status can be assessed during the cross-clamping period. RA can be performed in most patients, if so elected, unless there is a significant contraindication such as patient's refusal, cognitive limitation, anxiety, or language barrier. RA is accomplished by superficial cervical block using local anesthetics. Occasionally, small doses of intravenous narcotic or midazolam may be used, but the patient must remain awake and lucid during most of the procedure.

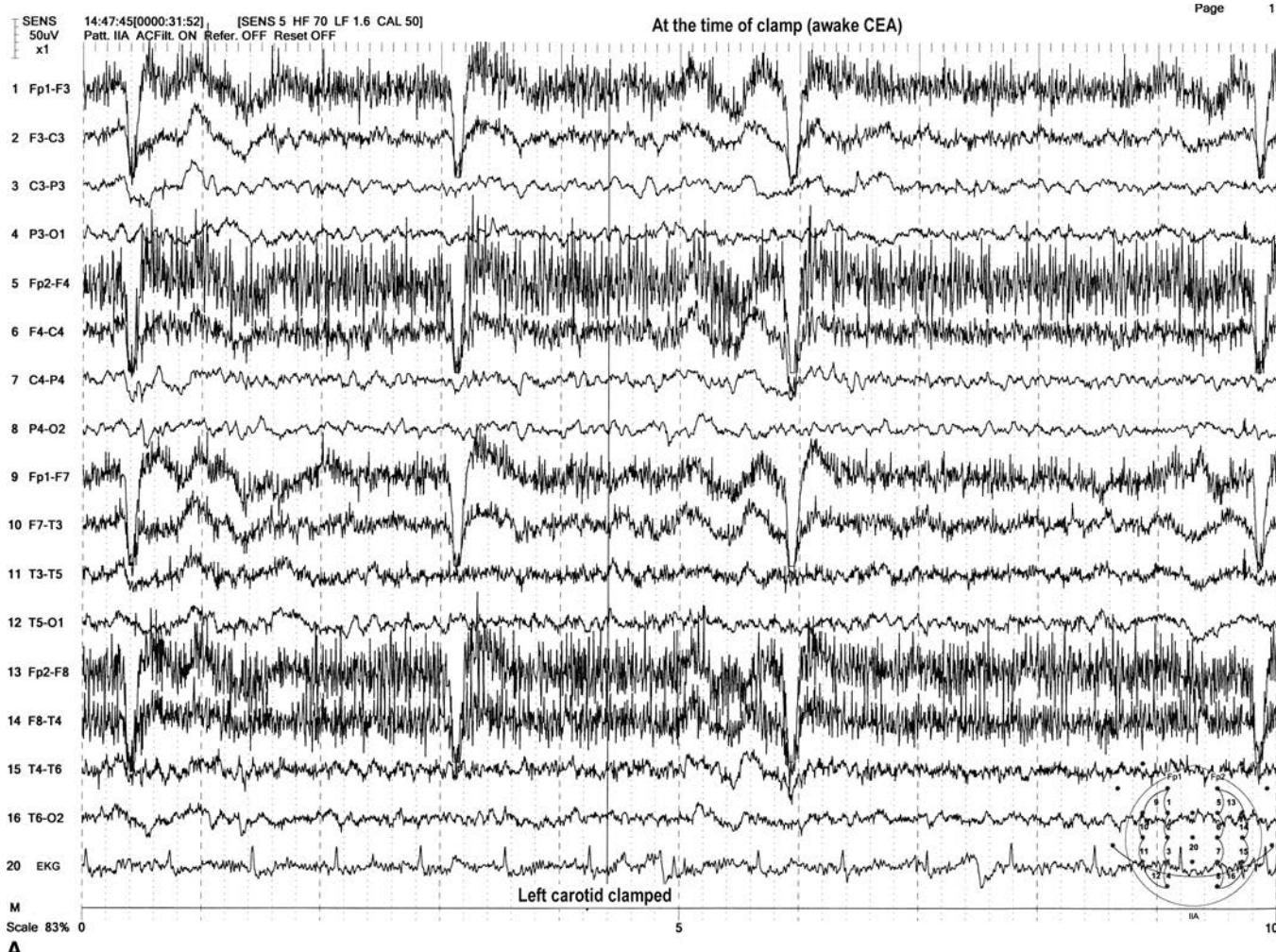
A relatively simple neurological examination involving speech, sensory and motor, and general cognitive functions can be tested when the patient is awake during the procedure. Perhaps this is the most reliable method to determine the necessity of shunt placement.

Based on EEG findings, the rate of shunt requirement under general anesthesia ranges from about 10% to 30%.<sup>14-17</sup> This rate is substantially higher than that of RA with the neurological examination in an awake patient, which is about 5% to 15%.<sup>16-20</sup> Does this mean that the EEG under general anesthesia is overly sensitive in warning of ischemic change, that is, excessive false-positive finding? Studies comparing EEG finding and neurological examination in awake patients during CEA showed that the EEG had a higher incidence of false-negative rates ranging from 30% to 40%, while false-positive findings were less than 10%.<sup>19,21,22</sup> Increased false-negative results for EEG in awake CEAs may be due to some difficulty assessing awake patients, because the EEG recording may have the extra noise of increased muscle or other artifacts and, at times, low-amplitude alpha rhythm or exceedingly low-amplitude background activity in awake patients who are anxious. The most sensitive EEG parameter is beta activity, which is commonly seen in general anesthesia. This may not be present in the awake patients (Fig. 6-5A to D). One should be aware of the important fact that the EEG monitoring protects only global ischemia and is not sensitive to ischemic changes or hypoperfusion limited to small cortical or subcortical regions such as capsular ischemia. One study raised a possibility that the awake state may make the brain less vulnerable to hypoperfusion and cerebral ischemia than the anesthetic state.<sup>21</sup> This appears to contradict the general assumption that anesthesia, especially deep anesthesia with burst suppression, protects the brain from cerebral ischemia by decreased metabolism. However, under general anesthesia, the relationship between EEG and postoperative neurological deficit appeared to be the opposite since more false-positive than false-negative EEG findings are noted<sup>6,23</sup>. These two studies suggested that the EEG under general anesthesia is overly sensitive for predicting cerebral ischemia.

### THE INCIDENCE OF STROKE AFTER CEA

An intraoperative stroke rate was reported to be 2.1% in the North American Symptomatic Carotid Endarterectomy Trial study,<sup>1</sup> in which no uniform method of intraoperative cerebral monitoring or protection was used. An overall incidence of perioperative stroke rate was reported to be 2% to 6%.<sup>8</sup> With EEG monitoring and selective shunting, the overall incidence of stroke was less than 1% as compared to the incidence of 2% to 4% in the nonmonitored/nonshunted group or routinely shunted group.<sup>24,25</sup>

The incidences of perioperative stroke with and without the presence of contralateral carotid occlusion or stenosis have been in dispute. Some studies reported greater incidence of perioperative stroke in patients with occlusion or stenosis of contralateral carotid artery than those without,<sup>8,26</sup> while others reported no difference between the two groups.<sup>9,27</sup> The highest incidence of perioperative stroke was found in patients with



**Figure 6-5. A–D.** An 83-year-old woman with history of stroke and TIAs affecting the left hemisphere has a 90% stenosis of the left carotid artery and a 50% stenosis on the right carotid artery. CEA was performed during the awake state with RA. **A:** The EEG showed preexisting delta activity over the left hemisphere. **B:** Within 30 seconds after the clamp, there were increases of delta slow waves and decreases of alpha-theta background activity over the left hemisphere. **C:** This persisted until a shunt was placed. Despite obvious EEG changes, the patient remained asymptomatic during the clamp period. **D:** Final recovery was achieved about 3 minutes after the shunt was placed. (From Yamada and Yeh. Monitoring EEG during carotid surgery. In: Schomer D, da Silva FH, eds. *Niedermeyer's Electroencephalography*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2011, with permission.)

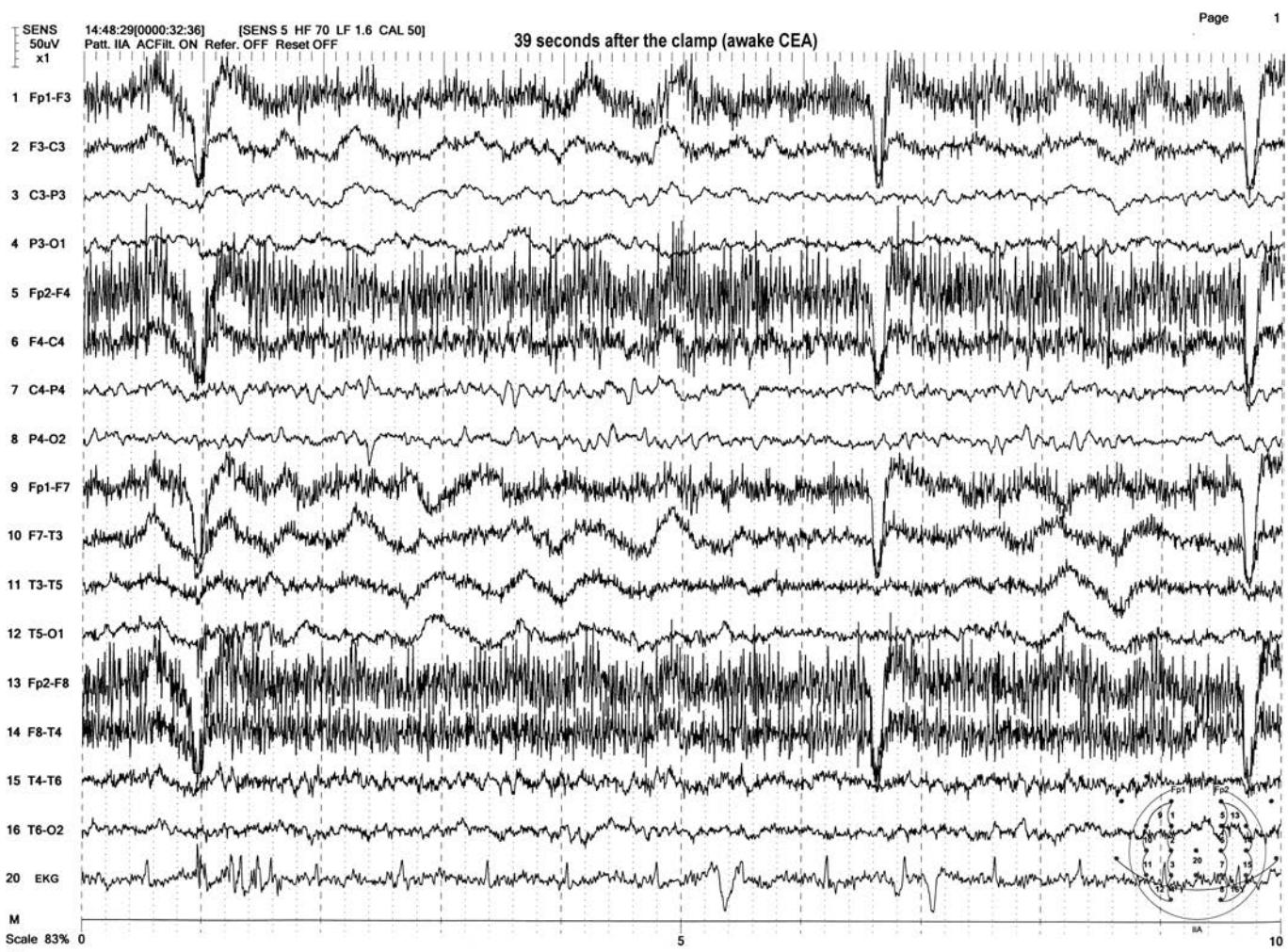


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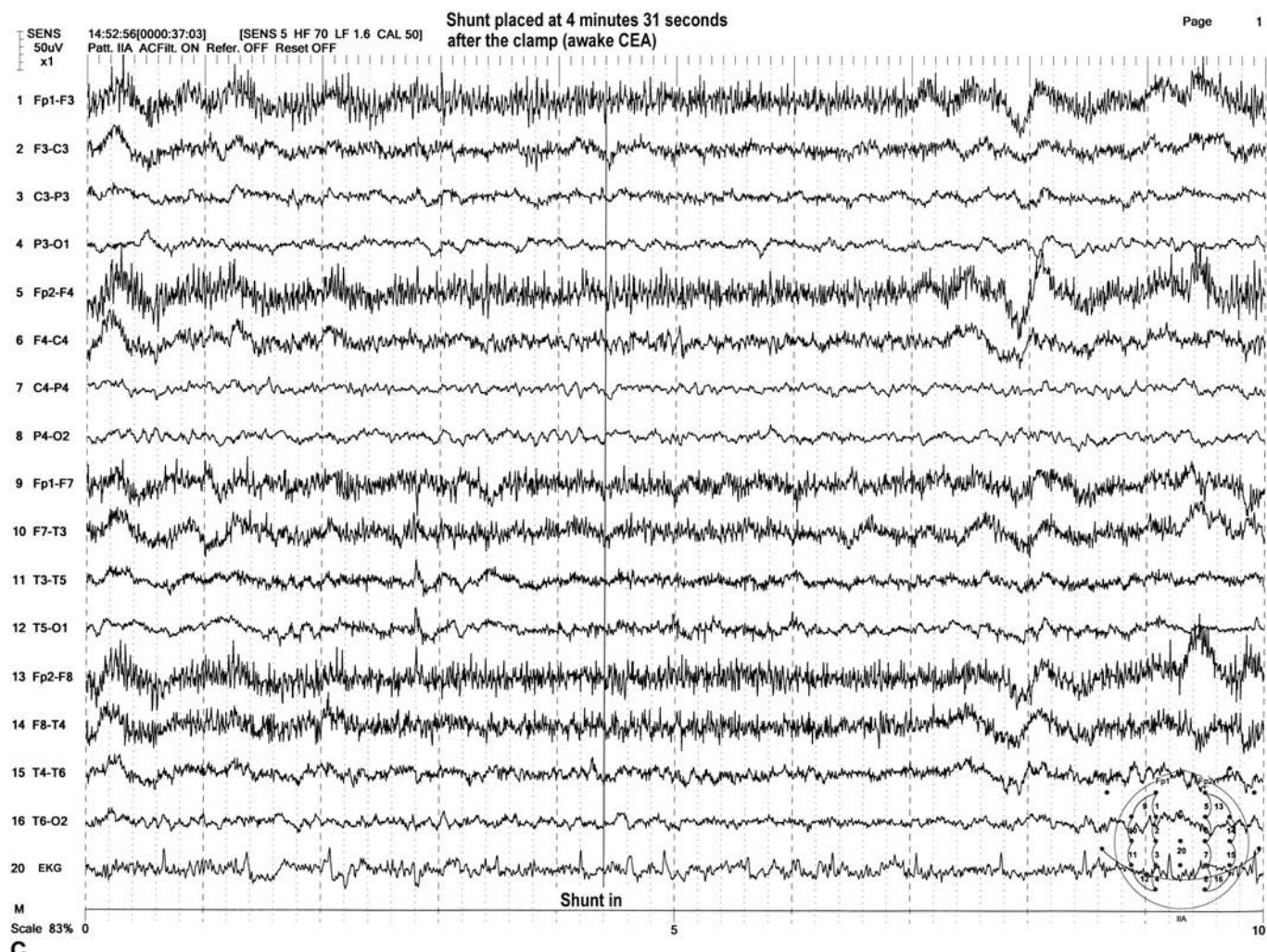


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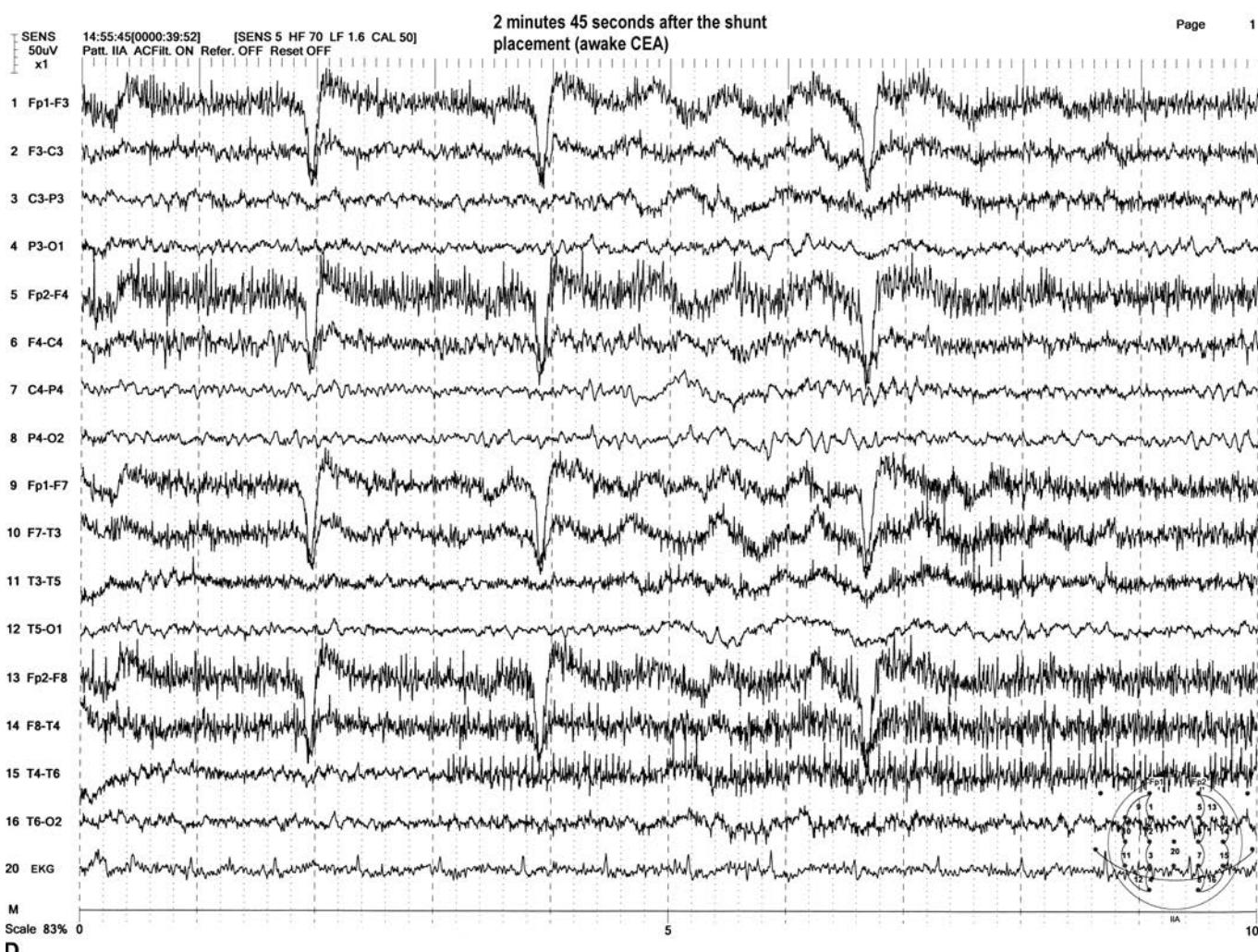


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occlusion of the contralateral carotid artery who also showed EEG changes.<sup>23</sup> Also, the stroke incidence was higher in patients with a history of previous stroke than those without.<sup>8,28</sup>

## THE USE OF SSEP FOR CEA

SSEP is dependent upon the integrity of sensory pathways starting from the peripheral nerve to the sensory cortex via the internal capsule and thalamus. Unlike EEG that is not sensitive in detecting small subcortical ischemia, SSEP can reflect ischemic changes occurring in small areas of the capsular region, which are important for neurological function. However, one should realize that the area covered by SSEPs is relatively small as compared to EEG.

One of the disadvantages of SSEP is the technical challenge of recording such small potentials in an electrically hostile environment common to an operating room. One encounters technical difficulties more often with SSEP recordings than with EEG recordings. Electrical noise or artifacts are relatively easy to recognize in the EEG recording because of its continuous nature. Artifact or electrical noise that is often difficult to identify can contaminate SSEP responses. These artifacts, in turn, can change the response making it appear as if real pathology is present. Unlike EEG that shows changes instantaneously, SSEP recordings require averaging the responses. Thus, there is a delay of a few minutes to yield one response and an additional few minutes' delay to verify the response changes. Another disadvantage of SSEP is that the recording often cannot be performed in patients who have peripheral neuropathy or impaired peripheral nerve conduction of the upper extremities, which is not uncommon in the elderly patient population. Nonetheless, SSEP monitoring has shown favorable results for the purpose of monitoring to detect cerebral ischemia.

Comparing the SSEP, EEG, and TCD in 156 patients, EEG yielded one false-negative and no false-positive results, and TCD showed four false-positive and no false-negative results, but SSEP had no false-positive or false-negative results.<sup>29</sup> The criterion used to determine the need for shunting was a greater than 50% amplitude reduction of the N20/P25 potential using median nerve SSEP. Using the same criterion, another study also supported the SSEP to be the most reliable in warning of ischemia, as compared to TCD or spectral-edge frequency analysis of EEG.<sup>30</sup>

There have been many other methods used for detection of cerebral ischemia. These include cerebral oxygen saturation study, carotid stump pressure, TCD, Xenon-133 washout study, and quantitative EEG.<sup>31</sup>

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# Spinal Cord Monitoring

## INTRODUCTION

Since the early 1990s, the accepted standard of care in surgeries involving the spine or the spinal cord has been the use of intraoperative monitoring (IOM) of spinal cord function in order to warn of potential injury and lessen the inherent risk involved.<sup>1</sup> Because of the ease of application and long history of its use, recording of somatosensory evoked potentials (SSEPs) was the only electrophysiological method used to monitor spinal cord function intraoperatively for many years. This allowed recording and measurement of sensory potentials arising from the sensory cortex and subcortical areas after peripheral nerve stimulation in the lower and upper extremities. These are reliable and reproducible signals that occur at predictable times after stimulation. In the operative setting, recording baseline values for these cortical and subcortical potentials allows comparison to later measurements as the surgery progresses.<sup>2</sup> These potentials, however, are sensitive to changes in doses and levels of anesthetic agents and to physiological and systemic variables including blood pressure, temperature, and CO<sub>2</sub>/O<sub>2</sub> balance.<sup>3</sup> The presence of intact SSEPs indicates integrity of sensory function during surgical manipulations, and adequate monitoring of these potentials requires knowledge of neurophysiology and neuroanatomy in order to accurately interpret changes so as to warn of the potential for postoperative neurological sequelae.

Over the past decade, monitoring motor function using transcranial electrical stimulation (TcES) has become more widely used as a complementary modality to SSEP monitoring and may have the potential to further decrease the risk of spinal cord injury by providing increased sensitivity of monitoring.<sup>4</sup> This is most often accomplished by recording compound muscle action potentials (CMAPs) from upper and lower extremity muscles after transcranial stimulation. Alternatively, some centers record spinal cord responses (referred to as D waves and I waves) from electrodes placed in the epidural space either percutaneously or after laminectomy or laminotomy.<sup>5</sup> Direct, or D waves, are evoked typically with a single stimulation (without averaging). The peak-to-peak amplitude of the D wave is monitored. A 50% or greater decrease in this amplitude is considered significant as it has been shown to correlate with the presence of a permanent motor deficit post-operatively.<sup>6</sup> In addition, spinal cord function can be monitored by stimulating the spinal cord using epidural electrodes and recording responses from the scalp, lower extremity muscles, or peripheral nerves.<sup>7,8</sup>

In addition to somatosensory and motor tract monitoring, the use of intraoperative electromyography (EMG) may assist in the evaluation of pedicle screw placement and vertebral integrity in spinal fusion or in tethered cord surgeries as well as in selective dorsal rhizotomies for the treatment of spasticity.<sup>9</sup> In spinal fusion and tethered cord surgeries, stimulated EMG as well as free-run EMG provides useful information in evaluating nerve root irritability.

Continuous online remote monitoring is generally considered a preferred method of IOM in which a physician appropriately trained in IOM is available for interpretation of the data on a continuous basis and has direct access to the surgical, anesthetic, and technical staff for trouble shooting purposes and conferencing.<sup>10</sup> In this setting, an appropriately trained technologist is in the operating room (OR) during the entire surgical case and typically prepares the case for the monitoring including electrode placement, physical arrangement of recording equipment, setting appropriate computer programs according to the laboratory protocol, making other technical modifications, and performing trouble shooting during the case whenever necessary.<sup>11</sup> It is critical that an operative log be kept electronically or in some other way during the procedure and that surgical events or manipulations such as opening, decorticating, placement of instrumentation or surgical hardware, as well as bone graft placement and closing are recorded. This log should also include information on anesthetic medications used during induction and maintenance, systemic parameters during baseline opening including mean arterial pressure, systolic and diastolic blood pressure, temperature, any blood loss, and administration of blood or blood products given. Manipulations of these parameters should be noted during the procedure so that neurophysiologic changes can be interpreted taking these into consideration.<sup>12</sup>

The technologist should have easy and readily available communication with the neurophysiologist, surgeons, and anesthesiologists involved. This communication may be through telephone access or other direct communication means throughout the duration of the surgical procedure as needed.

## SOMATOSENSORY EVOKED POTENTIALS

These evoked potentials are microvolts in amplitude and are recognized through the use of signal averagers that average out the “noise” or background activity that is not time locked (or is

unrelated) to the stimulus extracting those events that are related and time locked to the stimulus. Stimulation occurs for a range of averages, and in the OR, this may be 1,000 or more averages on each side. The greater the number of averages, the more improvement is seen in the signal-to-noise ratio<sup>3</sup> (see Chapter 1, pages 1–2, “Principles of averaging method” for further detail). However, the greater the number of averages, the longer each trial will take to collect, so this must be taken into consideration in the decision and planning of the surgery.

Either subdermal needle electrodes or cup electrodes (gold or silver-silver-chloride) are used for both recording and stimulating electrodes and are applied according to standard technique described elsewhere. Because subdermal needle electrodes have lower impedance than cup electrodes and are easily applied in the operating room, the subdermal needle electrodes are preferentially used for IOM. For recording of SSEP, scalp electrodes selected from the modified 10 to 20 electrode placement system are used with impedance kept below 5,000  $\Omega$ . This low impedance is important to reduce the stimulus and external interference artifacts that can make obtaining a reliable signal difficult.<sup>13</sup>

Amplification of the signal of interest occurs through the use of a differential amplifier that amplifies signals unique to its inputs but cancels out signals common to the two inputs involved. Typically, for systems involved in the OR, the common mode rejection ratio is 20,000 to 1, indicating the ability of the amplifier to reject signals common to the two inputs (see *Practical Guide: EEG*, Chapter 2, for further details).

Intraoperatively, multiple recording montages and sites allow for greater sensitivity of localization and for redundancy, both of which are important for adequate recording in this environment. The redundancy of electrodes is important because electrodes often become loose by body or head position changes during surgery. Typically, recording occurs from both upper and lower extremities. This can be accomplished by delivering a series of four sets of stimulations to the left and the right upper and lower extremities in close sequence and repeating the series until a sufficient number of averages is obtained (see Fig. 5-2). In this way, responses from all limbs are obtained within the same time frame. If monitoring changes occur, it is often necessary and prudent to run another average before confirming that the change in monitoring is significant and not due to artifact, technical factors, or other variables unrelated to the surgical manipulation.<sup>14</sup> This is where the experience and knowledge of the monitoring team cannot be overemphasized.

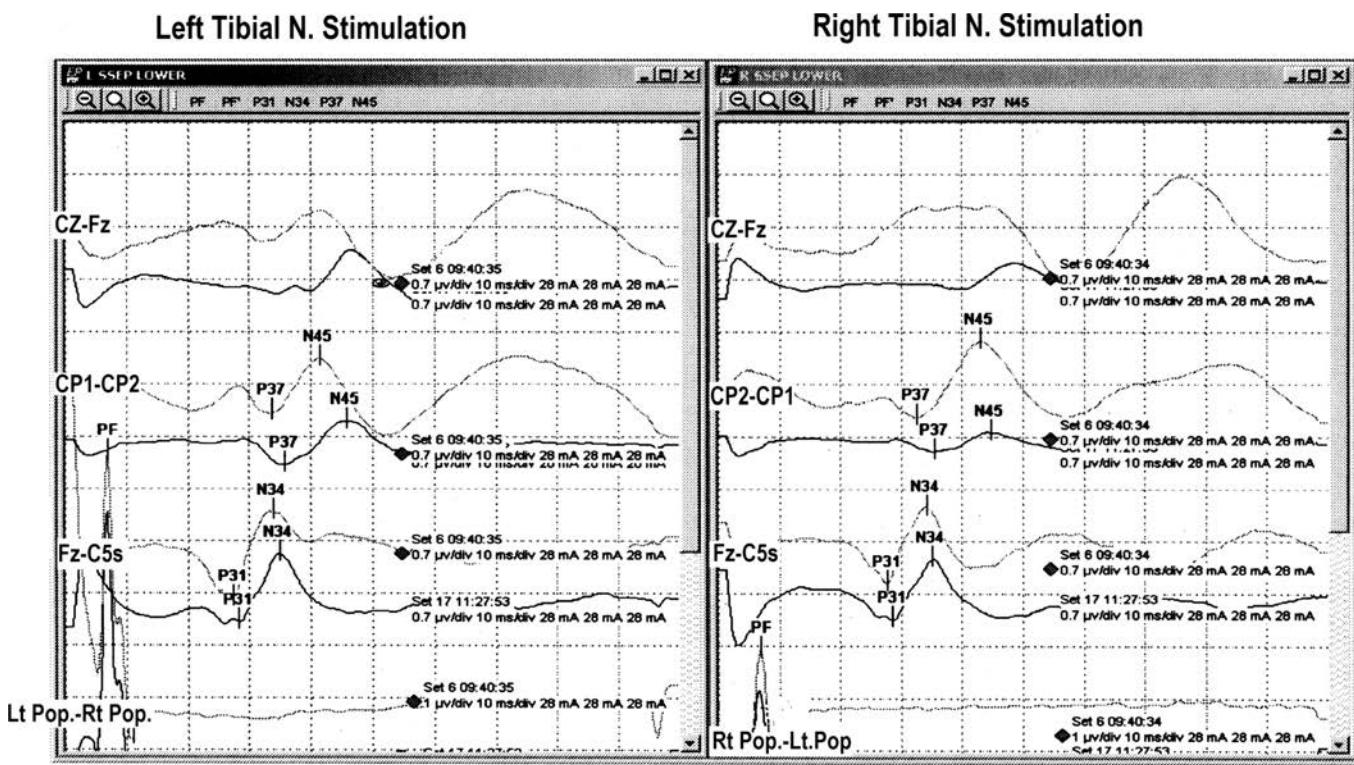
Any consistent change in latency may be significant depending on the progression of the change, although a 10% prolongation of the subcortical or cortical latency is generally considered abnormal. It is important to evaluate the peripheral response to see if it is prolonged as well.<sup>15</sup> If the peripheral response is prolonged, the change may be due to compression or ischemic change of the peripheral nerve being stimulated by prolonged stationary positioning of the limb. Alternatively, the prolongation of these latencies may be due to decrease in body or limb temperature. The limb can be adjusted by placing a roll under the extremity to change its position or warming cold limbs by use of warming devices. Warming devices unfortunately may often cause 60-Hz interference artifact. Notch filters must be left off because the frequencies involved in the SSEP may be affected. The filter also causes “60 Hz ringing,” which may contaminate short latency components of the response

(see Fig 1-14). A band pass of 30 Hz to 1 kHz (1,000 Hz) is recommended, but the high-frequency filter can be set to 500 Hz if there is excessive high-frequency noise. It is important to warn the surgeon of a change in the evoked potentials as soon as it has been verified as reliable and significant.<sup>16</sup> This should take less than 5 minutes as it is critical that the warning be timely and prompt, in order to prevent irreversible injury. Several hundred to a thousand collections are made for every SSEP average, and, unless there have been a significant number of artifacts in the response, it would be reliable.<sup>17</sup>

If the peripheral latency is unchanged and the latency prolongation occurs at the subcortical level, this may indicate that an ischemic or a vascular process is evolving. This should result in a warning to the surgeon along with correlation with the surgical events at that time. The latency changes can be unilateral or bilateral in nature. When the latency prolongation occurs only at the cortical level, it is important to exclude an assortment of variables that may be involved. These include anesthetic changes, including adjustment or addition in an anesthetic infusion or use of a new anesthetic agent or bolus of an existing or new anesthetic agent.<sup>18</sup> Latency prolongation can also be due to changes in the mean arterial pressure (typically a lowering), or a decrease in core temperature, or significant blood loss. An example of changes in SSEPs seen in the setting of decreased mean arterial pressure is illustrated in Figure 7-1. If the prolongation is unilateral in nature, it is unlikely to be a consequence of a systemic variable, and therefore the surgeon should be informed that a change in the monitoring potentials has occurred and this should be correlated with the surgical process.<sup>19</sup> In cases in which the latency prolongation of subcortical/cortical potentials is bilateral but one side appears to be more affected or prolonged than the other side, that side may be more sensitive to the systemic variables. Amplitude changes in the waveforms at the peripheral, subcortical, and cortical levels are also evaluated. A greater than 50% change in amplitude is generally considered significant, although any consistent change may be significant and would warrant an evaluation and review of possible variables involved in creating this change.<sup>20</sup>

## UPPER EXTREMITY SSEP MONITORING

Upper extremity stimulation typically involves stimulation of the median nerve, although the ulnar nerve can be used as an alternative. For lower cervical spine or spinal cord surgery, ulnar nerve stimulation is preferred because it reflects a lower cervical spine level than the median nerve, although median nerve SSEP responses in general have greater amplitudes than ulnar nerve SSEP responses. Peripheral electrical stimulations are usually delivered at the wrist but if this is not accessible, the forearm, antecubital or cubital fossa may be stimulated. The peripheral action potential can be recorded at the peripheral nerve with an electrode placed at Erb’s point (located at the supraclavicular fossa). In addition to the cortical potentials, the scalp recorded SSEP includes far-field potential components originating from the subcortical regions<sup>2</sup> (see Chapter 4, pages 55–56, “Generation mechanism of far-field potential(FFP)” for further details). Redundancy in neurophysiologic intraoperative monitoring (NIOM) is a good approach, so it is typical to obtain two cortical channels just in case one of the channels cannot be recorded. It is also valuable to confirm a change in this second channel if a change is thought to be present in the other channel.



**Figure 7-1.** Example of prolongation of the cortical and subcortical responses as a result of a significant lowering in mean arterial blood pressure. Note significant prolongation of subcortical potential of P31/N34 and cortical potential of P37/N45 with unchanged popliteal potential. (Darker tracing from each channel is the response after blood pressure drop.)

A suitable intraoperative upper extremity SSEP study could consist of the following channels (Fig. 7-2) (the peak of interest for that channel is in parentheses):

Epi-Epc	Ipsilateral Erb's point referred to contralateral Erb's point (N10)
C5s-Epc	C5 spinous process referred to contralateral Erb's point (N13)
CPi-Epc	Ipsilateral CP referred to contralateral Erb's point (P9, P11, P13/P14, N18)
CPc-Ci	Contralateral CP referred to ipsilateral CP (N20)

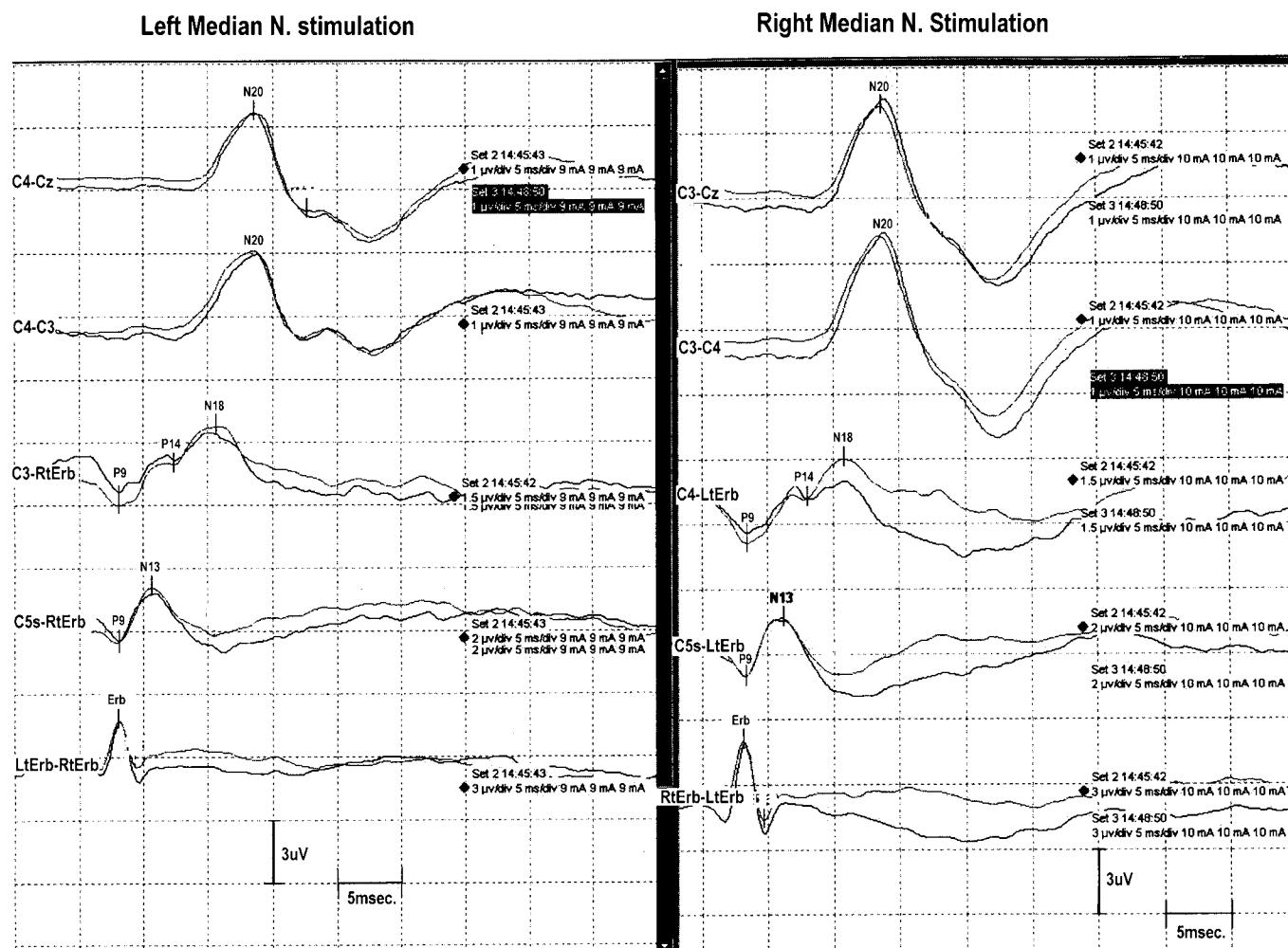
An alternative montage (see Chapter 4, Fig. 4-13A and B) is

Epi-Epc	Ipsilateral Erb's point referred to contralateral Erb's point (N10)
CPc-Fpz	Contralateral CP referred to Fpz (N20)
Fc or CPi -Ai	Contralateral F3 (CP3) or F4 (CP4) referred to ipsilateral ear (P13/P14, N18)
CPc-Ai	Contralateral CP referred to ipsilateral ear (P13/P14, N20).

Absolute latencies are dependent on arm length (see Chapter 4, Appendix Figs. 4A-1 to 4A-12), but interpeak latency measurements allow for a more reliable measure of central conduction times by limiting the effects of peripheral conduction times. In intraoperative recordings, baseline (control) responses are obtained after stabilized anesthesia but before the surgical manipulations have started. Comparison of latency from baseline values during the surgical procedure is the basis for

interpretation of an intraoperative change.<sup>21</sup> Recording an upper extremity SSEP, even in cases of thoracic/lumbar surgeries, can be useful and enhances the ability to troubleshoot in case the lower extremity SSEP is lost or changed.<sup>22</sup> For example, in thoracic/lumbar surgery, loss of both upper and lower extremity SSEPs suggests that the changes are more likely due to systemic effect rather than a spinal cord injury or ischemia. However, a loss of lower extremity SSEPs with unchanged upper extremity SSEPs strongly suggests thoracic/lumbar cord impairment. Erb's potential has an average latency of 10 ms (N10) in adults and can be used for the confirmation of effective stimulation delivery. When Erb's potential is absent in patients with severe polyneuropathy, however, scalp recorded cortical potential, especially the later cortical components, still may be present and can be monitored. However, one should be aware that the cortical components, especially the later components, are less consistent than the subcortical components and more susceptible to anesthetic or systematic changes.<sup>23</sup>

The potential recorded from C5 spine referenced to Epc is a cervical potential (N13), originating from interneurons of the dorsal horn of the cervical cord<sup>24</sup> and is more resistant than the cortical potentials to the effects of anesthetic agents. However, cervical recording cannot be used in cervical cord/spine surgery because the electrode location is usually within the surgical field. In this case, the subcortical potentials need to be relied on. The CPi-Epc montage registers all subcortical far-field potentials, that is, P9, P11, P13/P14, and N18. Of all these subcortical potentials, P14 and N18 originate from the brainstem and are important obligate potentials to follow



**Figure 7-2.** This is an example of an intraoperative upper extremity SSEP study with stimulation of the median nerve at the wrist. Channel 1 registers cortical potential N20 and channel 3 registers subcortical potential P14/N18. Channels 4 and 5 record cervical potential N13 and Erb's potential N10, respectively.

during monitoring (see Chapter 4, pages 57–61, “Short latency upper extremity SSEP”). CPc-Cpi montage registers the cortical potential at a latency of approximately 20 ms (N20). Perhaps the most important and useful evoked potentials in SSEP monitoring are the P14 and N18 subcortical potentials because they are relatively resistant to anesthesia and are the most consistently recordable potentials.<sup>24</sup> In an alternative montage, CPc-Fz registers N20 cortical potential that is accentuated by P20 from the Fz electrode. Fc-Ai records P13/P14 and N18 subcortical (far-field potential), and CPc-Ai registers P13/P14 subcortical and N20 cortical potentials. Figure 7-3A shows an example of loss of median nerve SSEP during intramedullary cervical cord tumor surgery. Figure 7-3B is the comparative preoperative median SSEP study in this patient. Shortly after the posterior myelotomy, the SSEP obtained with right-sided stimulation was abruptly lost. The surgeon was informed, but unfortunately the SSEP did not recover postoperatively. The preoperative SSEP was normal (Fig. 7-3B). The postoperative SSEP showed total absence of subcortical (P14) and cortical (N20) waveforms to right-sided stimulation (Fig. 7-3C). The patient had severe proprioceptive sensory loss in the right arm without a motor deficit.

## LOWER EXTREMITY SSEP MONITORING

Recording lower limb SSEPs (Fig. 7-4) is typically done with stimulation of the posterior tibial nerve at the ankle so that suitable channels in the operating room would be

PFd-PFp: This channel records N8 peripheral action potential at the popliteal fossa. Active and reference electrodes are placed in the popliteal fossa (N8) (d = distal and p = proximal)

Fz-C5s: This channel records subcortical potentials of P31 and N34

CPz-Fz: This channel records a large positive-negative cortical potential with latency approximately 37 ms (P37) and 45 ms (N45 or N50)

CPi-CPc: This channel also registers a large positive-negative cortical potential with latency approximately 37 ms (P37) and 45 ms (N45 or N50) (CPi and CPc refer to CP1 or CP2, ipsilateral and contralateral to the side of stimulation, respectively)

An alternative montage is as follows:

PFd-PFp: This registers N8 peripheral action potential  
CPz-(A1 + A2)

or -A1 or A2: This channel registers the subcortical potential (P31) and cortical potentials (P37 and N45 or N50)  
 CPi-(A1 + A2)

or -A1 or A2: This channel also registers the subcortical potential (P31) and the cortical potentials (P37 and N45 or N50) (CPi refers to CP1 or CP2, ipsilateral to the side of stimulation)

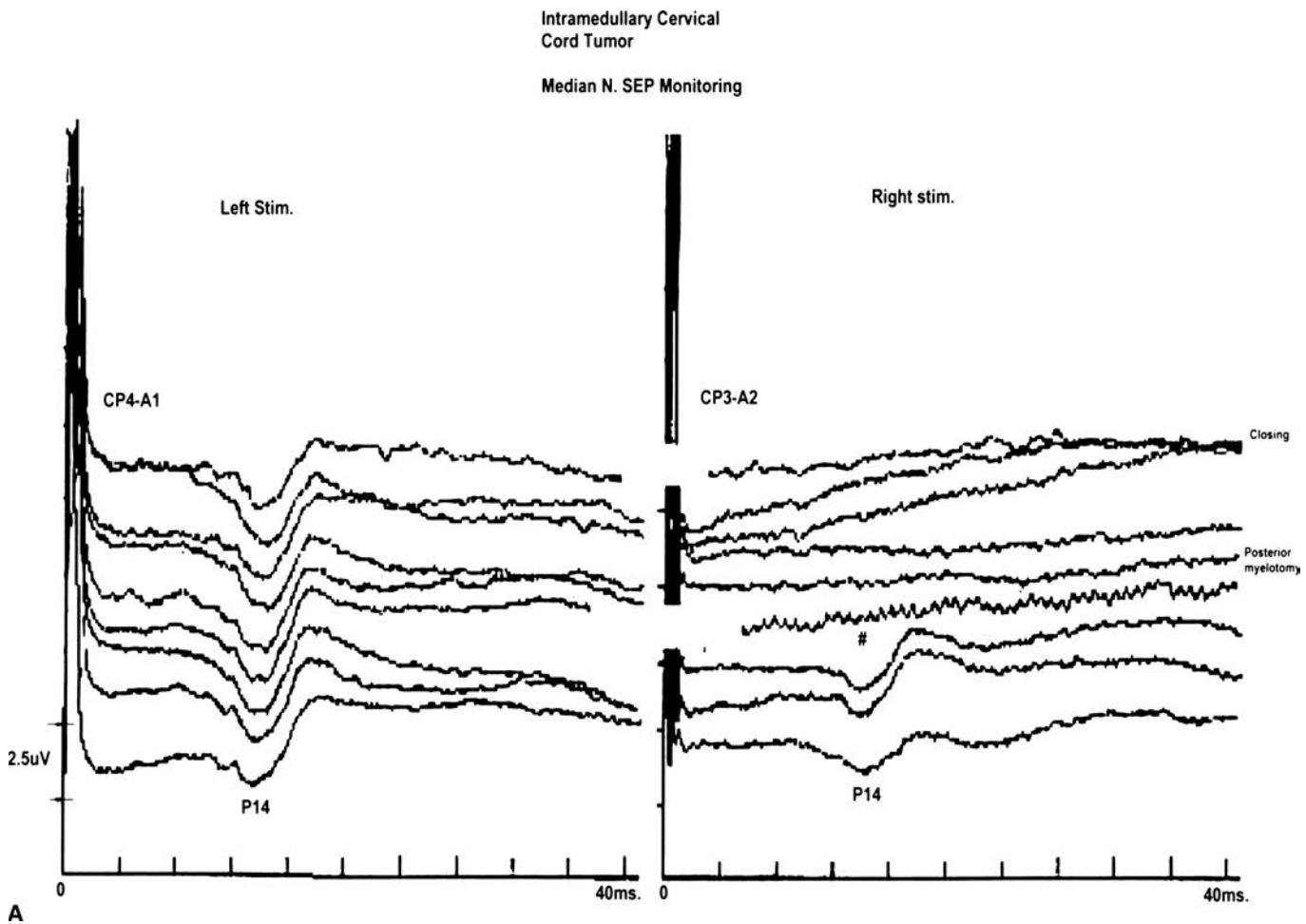
CPz-Fz: This channel registers P37 and subsequent negative N45 or N50 potentials

If the ankle is not accessible, the posterior tibial nerve or the peroneal nerve can be stimulated at the popliteal fossa, but this may cause vigorous leg twitches. The response from the peroneal nerve is typically of lower amplitude than that from the tibial nerve.

The most consistent and reliable component under anesthesia is P31, which is the equivalent potential to P14 of the upper extremity SSEP. Unlike P14, however, P31 may not be recorded (nonobligate potential) in preoperative baseline studies during awake recordings. Nonetheless, P31 is usually present during anesthesia, most likely due to decreased muscle artifact and the

ability to use greater stimulus intensity. An additional electrode at CP1 or CP2, although redundant, may allow the P37 cortical component to be better delineated at CP1 or CP2 than at the CPz electrode in some subjects. Because of paradoxical lateralization (see Chapter 4, page 68, "Paradoxical lateralization") of the lower extremity SSEP, CP1 should be used for the left tibial nerve stimulation and CP2 should be used for the right tibial nerve stimulation.

Figure 7-5 shows a case of SSEP changes during scoliosis surgery. Sudden loss of SSEPs is seen bilaterally. After verifying that the change was reproducible and not due to technical or systemic variables, the surgeon was informed. A wake-up test was performed in which the patient was found able to move hands but not toes. The spine distraction then was then eased and recovery of SSEPs was noted without development of postoperative deficit. Figure 7-6A demonstrates SSEP changes occurring during a case involving intramedullary spinal cord tumor removal. Shortly after tumor removal, sudden and consistent loss of posterior tibial SSEPs was noted bilaterally. The surgeon was informed and steroids were given. Loss of the SSEP remained at the end of surgery and the patient had severe loss



**Figure 7-3. A:** An example of median nerve SSEP during intramedullary cervical cord tumor removal. Shortly after the posterior myelotomy, there was sudden loss of SSEP only to the right median nerve stimulation. (From Yamada T, Tucker M, Husain A. Spinal cord surgery. In: Husain AM, ed. *A Practical Approach to Neurophysiologic Intraoperative Monitoring*. New York, NY: Demos, 2008:117–137 (Chapter 8), with permission.) **B,C:** Same patient as A. Preoperative SSEP was normal bilaterally (**B**) but postoperative SSEP showed absence of subcortical potentials (P14/N18) and cortical potential of N20 in association of normal cervical N13 and Erb's potential to the right-side stimulation (**C**). The patient had severe loss of proprioceptive sense of right arm but with preserved motor strength. (From Yamada T, Tucker M, Husain A. Spinal cord surgery. In: Husain AM, ed. *A Practical Approach to Neurophysiologic Intraoperative Monitoring*. New York, NY: Demos, 2008:117–137 (Chapter 8), with permission.)

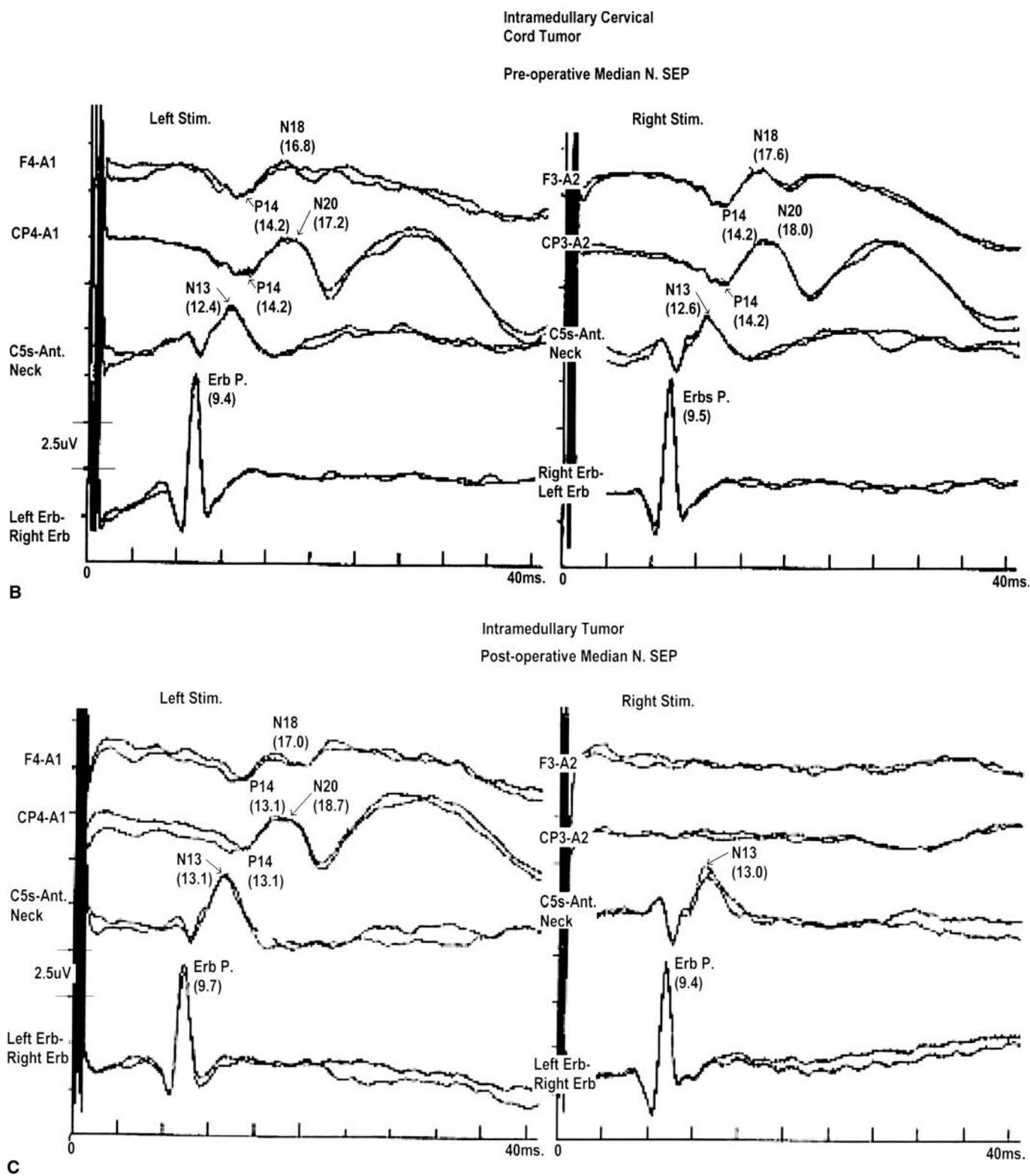
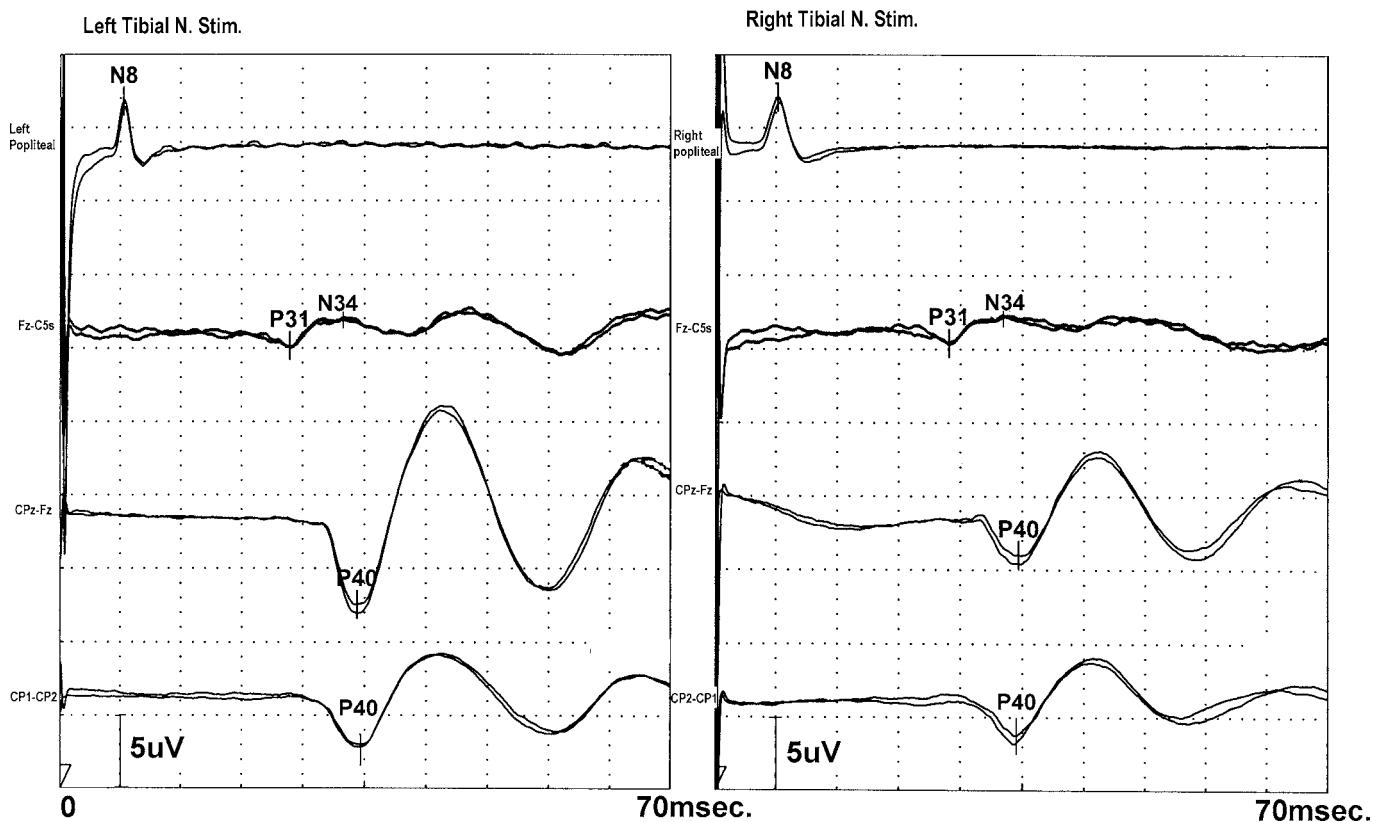


Figure 7-3. Cont'd.



**Figure 7-4.** This is an example of a lower extremity intraoperative SSEP study with stimulation of the posterior tibial nerve at the ankle. Channels 3 and 4 register the cortical potential of P37 and N45 (N50). Channel 2 registers subcortical potentials of P31 and N34. Channel 1 is for peripheral nerve potential at the popliteal fossa.

of proprioceptive sensation in both legs with minor paraparesis. Preoperative SSEP was normal (Fig. 7-6B), but postoperative SSEP showed no cortical responses, bilaterally (Fig. 7-6C).

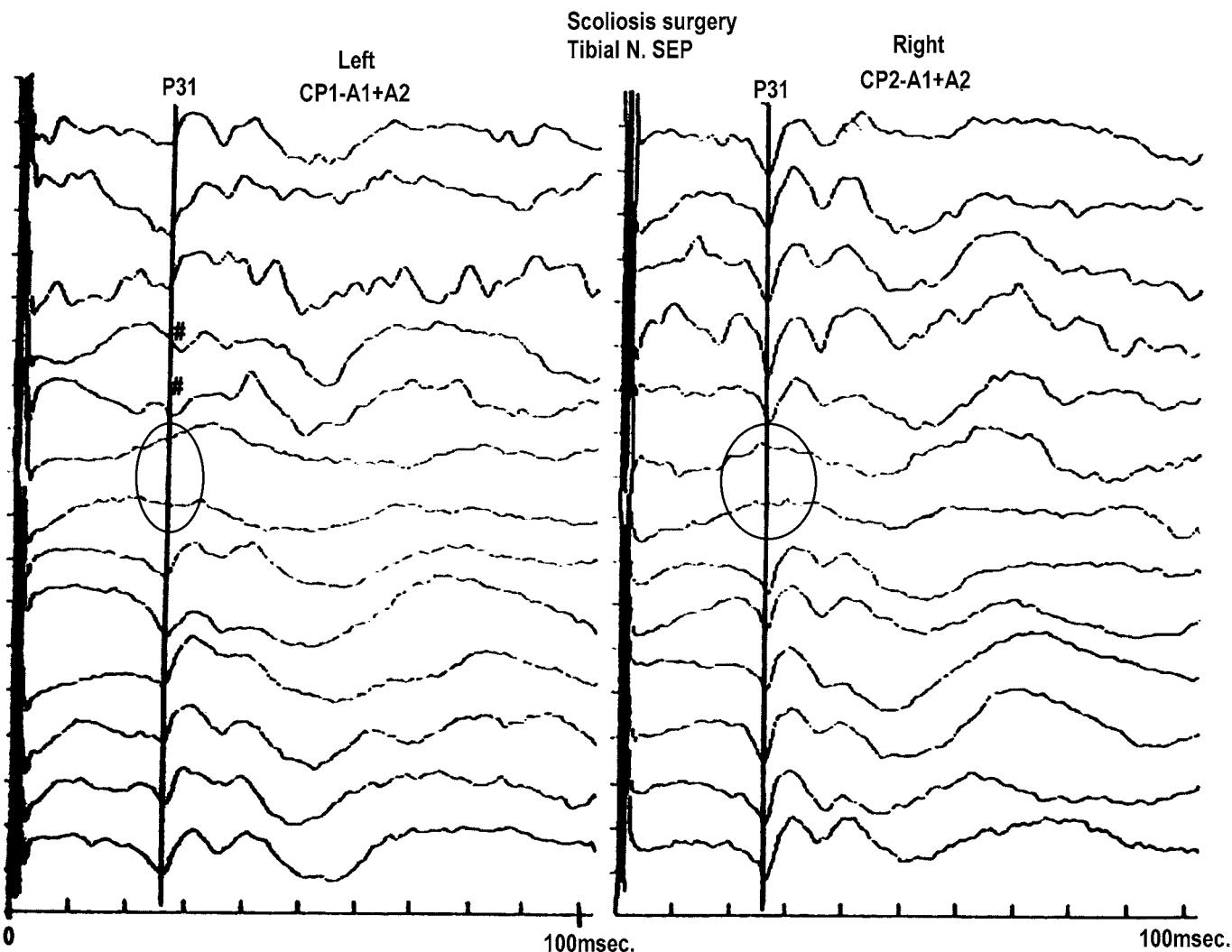
## TRANSCRANIAL ELECTRICAL MOTOR STIMULATION

The successful presence of muscle responses after TcES correlates to intact postoperative motor function, and its absence or loss during a surgical case corresponds with a high degree of sensitivity to impaired motor function. In fact, TcES will be affected in most cases prior to any change noted on SSEP monitoring although not always; hence, the monitoring of both modalities during surgeries is recommended whenever possible. Sometimes, TcES is utilized to modify the extent of tumor resection. The presence of intact motor evoked potentials (MEPs) allows the surgeon to continue with the resection with greater confidence that intact motor function is preserved. TcES is done through a multipulse stimulating technique involving a short train of three to five electrical stimuli applied to the scalp and transcranial stimulation of the motor cortex using needle or cork screw-type electrodes (which tend to have lower impedance). In very young children in whom there is concern over the presence of a fontanel, EEG cup electrodes may be used. The recording of CMAPs or MEPs from limb muscles is made using subdermal needle electrodes in the upper and lower extremities bilaterally.<sup>25</sup> Although surface cup

electrodes could be used on the limbs for recording MEPs, in our experience, they pose more difficulties. The impedance is higher, and therefore an increased stimulation intensity is required. The increased stimulus intensity increases the likelihood of stimulus artifacts. Figure 7-7 is an example of transcranial motor stimulation with recording of MEPs from the upper and lower extremities.

The motor cortex is best identified 1 to 2 cm anterior to the CZ electrode using the International 10 to 20 System of Electrode Placement. Some laboratories have used 2 cm anterior to C3 or C4 alternatively. In theory, anterior to C3 or C4 may be optimal in order to obtain reliable upper extremity MEP responses and anterior to CZ is optimal to obtain lower extremity MEP responses, but in practice, C3 and C4 electrodes are usually successful in recording both upper and lower MEPs simultaneously. The polarity of stimulus dictates which hemisphere is preferentially stimulated, so that the hemisphere under the anode side is predominantly stimulated (anodal stimulation). This is in contrast to peripheral nerve stimulation in which the cathode electrode is the site of activation. If the anode electrode is C3 and the cathode is C4, this will cause a CMAP from extremities on the right side, and alternatively if C4 is the anode and C3 is the cathode, the CMAP will be obtained from the left side (see Fig. 7-7). However, it is not uncommon to be able to elicit CMAPs from muscles on both sides simultaneously.

Typically, greater stimulus intensity is needed to obtain responses from the lower extremities than from the upper



**Figure 7-5.** This is a case of a lower extremity intraoperative SSEP study in which an SSEP change was noted during scoliosis surgery. During the instrumentation of the spine, there was sudden loss of SSEP bilaterally. The SSEP loss was verified by repeating it (shown by circles). The change was discussed with the surgeons and wake-up test was done. During the wake-up test, the patient was able to move her arms but not her feet. The surgeons then decided to lessen the spine distraction and the SSEP returned bilaterally. The patient had no neurological deficits.

extremities. The voltage should be incrementally increased until motor responses are obtained. MEPs can be elicited by a single stimulus and signal averaging is not required. The required stimulus intensity varies depending on the subject, anesthetic agents, or yet unknown factors, but it is generally 200 to 800 V with a current of 300 to 1,000 mA and a duration of 0.1 to 0.2 ms. In some cases, greater than 1,000 mA is required to elicit measurable MEPs. MEPs can be elicited with lower stimulus intensities when total intravenous anesthesia (TIVA) rather than inhalational anesthesia is used (see the section "Anesthesia during MEP and SSEP monitoring"; see also "Anesthesia Considerations" in Chapter 5).

The use of a stimulus train of three to five stimuli is generally more effective than the use of a single stimulation. The interstimulus interval (ISI) range is 1 to 4 ms. There can be a great deal of patient variability in the ISI which allows the most reliable MEPs to be obtained. The choice of ISI is related to the optimal discharge of corticospinal tract neurons that may be

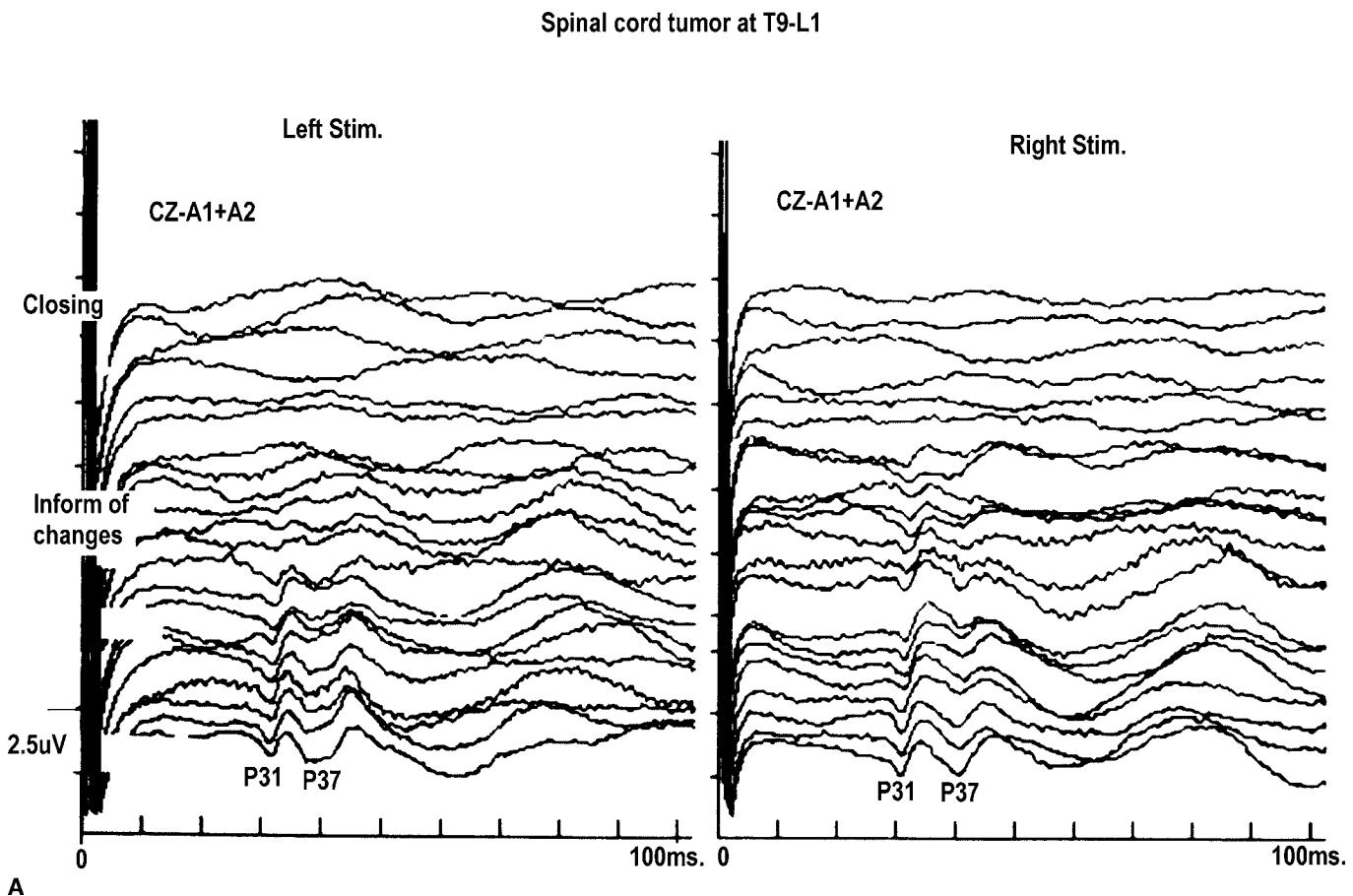
refractory to electrical stimulation if the ISI is too short.<sup>26</sup> If there is no great variation in anesthetic, muscle relaxant, or temperature, MEP responses should be reproducible and can be seen reliably at similar latencies and amplitudes, although the waveform configurations may change.<sup>27</sup> Unfortunately, the operating room often does not allow these variables to remain constant, and these responses may not have reproducible latencies or amplitudes. In some cases, MEPs cannot be elicited at all immediately after recording a well-defined MEP in the absence of a change in the stimulus, recording parameters, or physiological conditions. The reason for this inconsistency is not definitely known. Amplitude reduction of greater than 50% has generally been considered a warning sign of potential neurological compromise. If anesthetic and physiologic variables are not consistent, significant amplitude fluctuations can be seen on that basis alone. Additionally, there is an inherent variability in MEP amplitudes. This may be based on the excitability of the motor neuron pool although this variability is

typically well below the warning threshold. Therefore, defining an abnormality should be based on consistent depression (>50%) or persistent absence of the response.<sup>27</sup>

Utilizing more than one muscle in the upper extremity and more than one muscle in the lower extremity is useful to provide consistency and allow for evaluation over greater motor segments, thereby increasing the ability to detect changes. A reasonable protocol for monitoring may involve distal as well as a proximal muscle recording from each limb bilaterally. In the upper extremity, the abductor pollicis brevis and brachioradialis muscles are easily identified and would be a good choice. In the lower extremity, the tibialis anterior, gastrocunemius, vastus lateralis, rectus femoris, or abductor hallucis muscles are easily identified and provide good responses in most cases.

Since there is a great variation in response amplitudes, amplification is used to improve visualization of the recordings. Typically, the sensitivity may be at 50 or 100  $\mu$ V and this is adjusted as needed. Baseline responses are obtained prior to incision and after the anesthetic agents used for induction have worn off. It should be noted that MEPs are much more sensitive to anesthesia than SSEPs. With the same level of an-

esthesia, therefore, MEPs could be lost, but SSEPs may remain unchanged. If the MEP changes occur in both upper and lower extremity muscles in thoracic or lumbar cord/spine surgery, this is more likely the result of a systematic or a global effect resulting from blood loss, anesthesia, temperature changes, etc. Greater concern over spinal cord injury would be present when an MEP change occurs on one extremity or starts in one extremity, before involving another extremity. Correlation with the other limbs and with SSEPs should be evaluated promptly, so interpretation can be made and discussion with the surgical staff accomplished within minutes in order to avoid permanent neurological sequela. An example of this type of abnormality is shown in Figure 7-8A–D. The patient in this example underwent removal of an intramedullary and extramedullary spinal cord tumor at T12 to L2 spine. Shortly after the removal of the tumor, MEPs were lost from the right tibialis anterior and abductor hallucis muscles, while other MEPs and the SSEPs remained unchanged. These changes were discussed with the surgeons. There was no recovery of MEP by the end of surgery, and postoperatively the patient was found to have right leg weakness without a sensory deficit.



**Figure 7-6.** A: In this case, the lower extremity intraoperative SSEP is recorded for intramedullary spinal cord tumor involving T9-L1 spinal cord. Shortly after the removal of the tumor, there was loss of SSEP bilaterally. This was discussed with the surgeon and a steroid infusion was administered, but no recovery of the SSEP occurred. B,C: Same patient as A. Preoperative SSEPs showed normal cortical (P37) and spinal (N24) potentials, bilaterally. Postoperatively, there was loss of the cortical potential P37 bilaterally. The patient was found to have paraparesis and sensory loss involving both lower extremities.

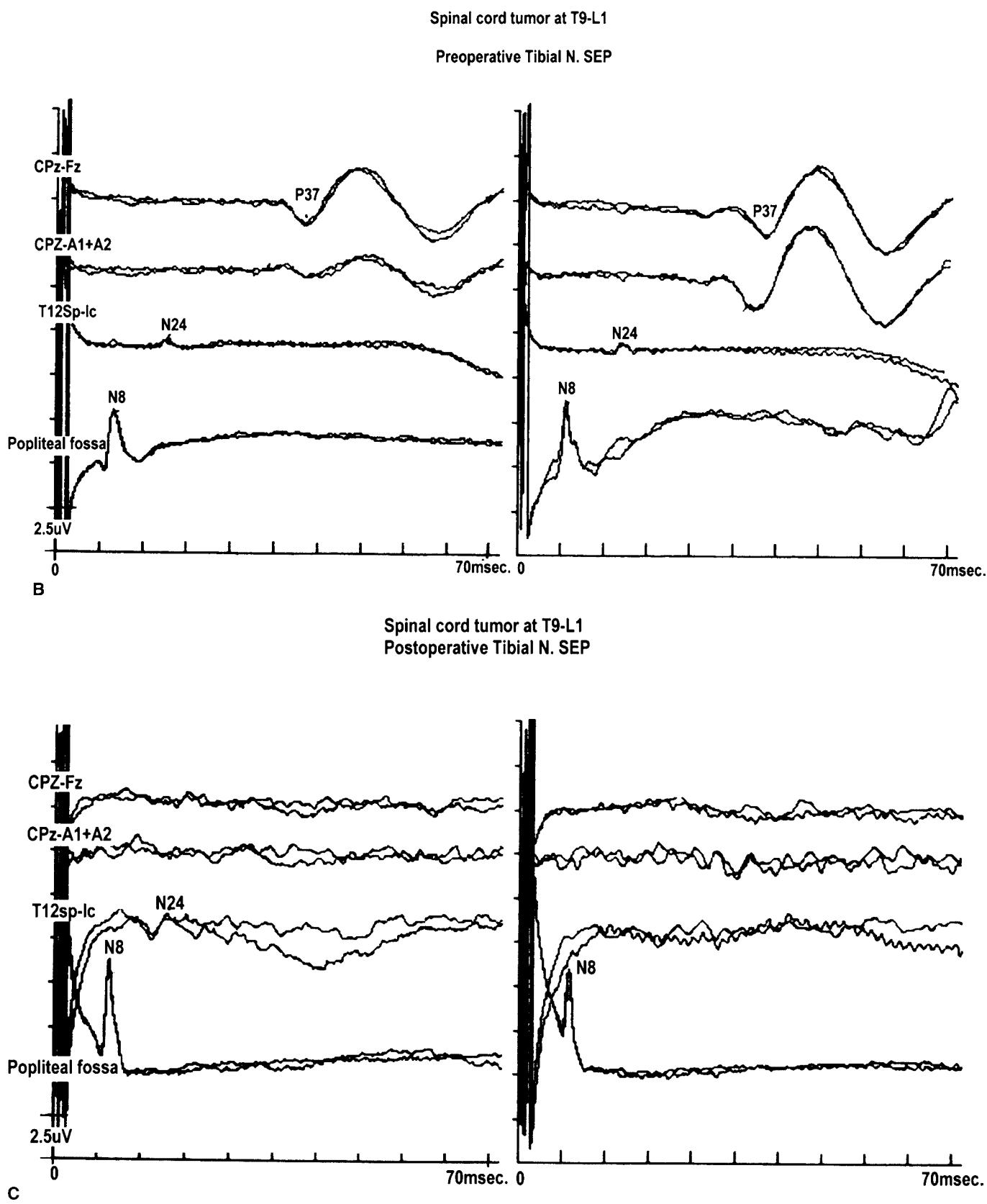
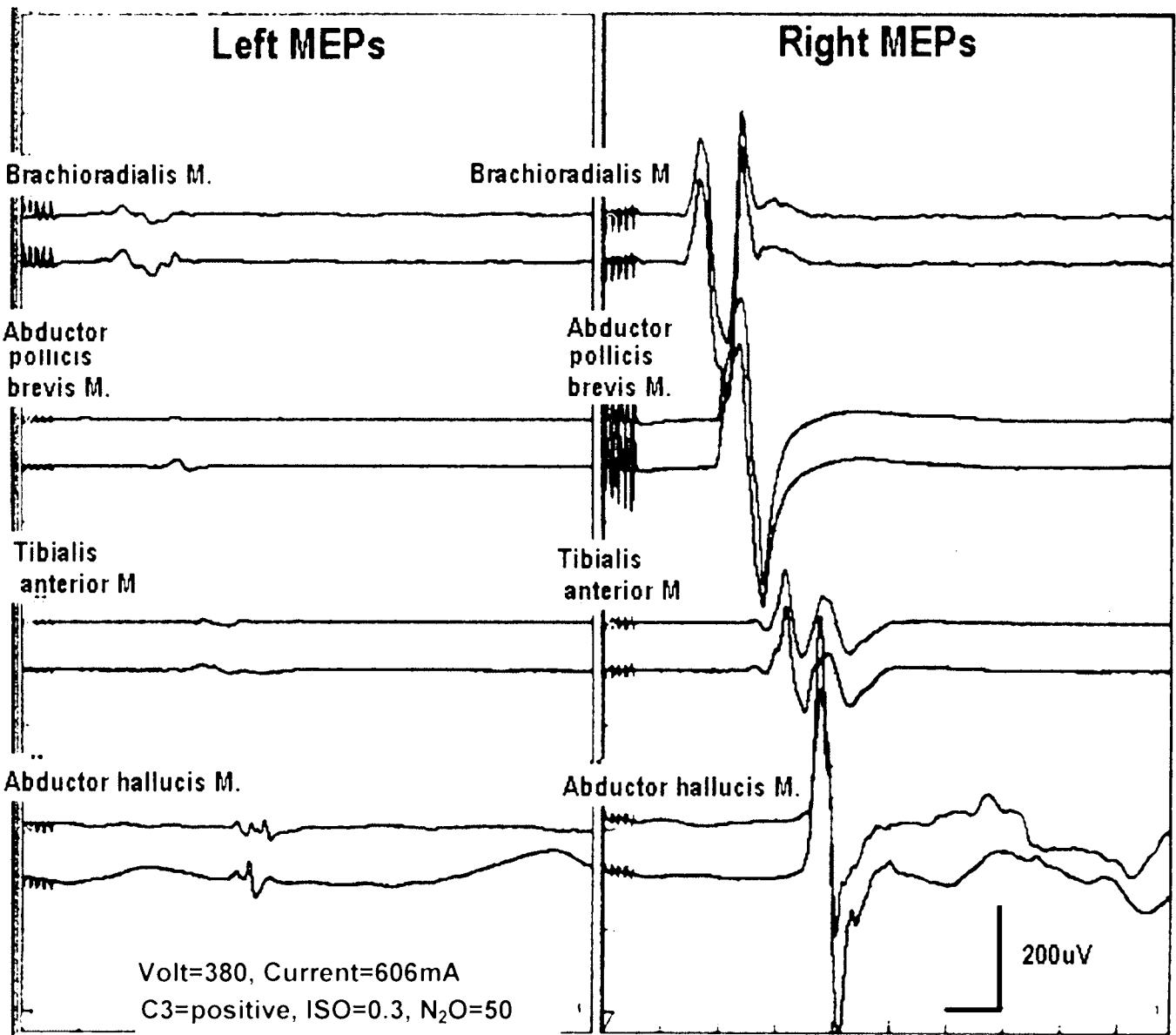


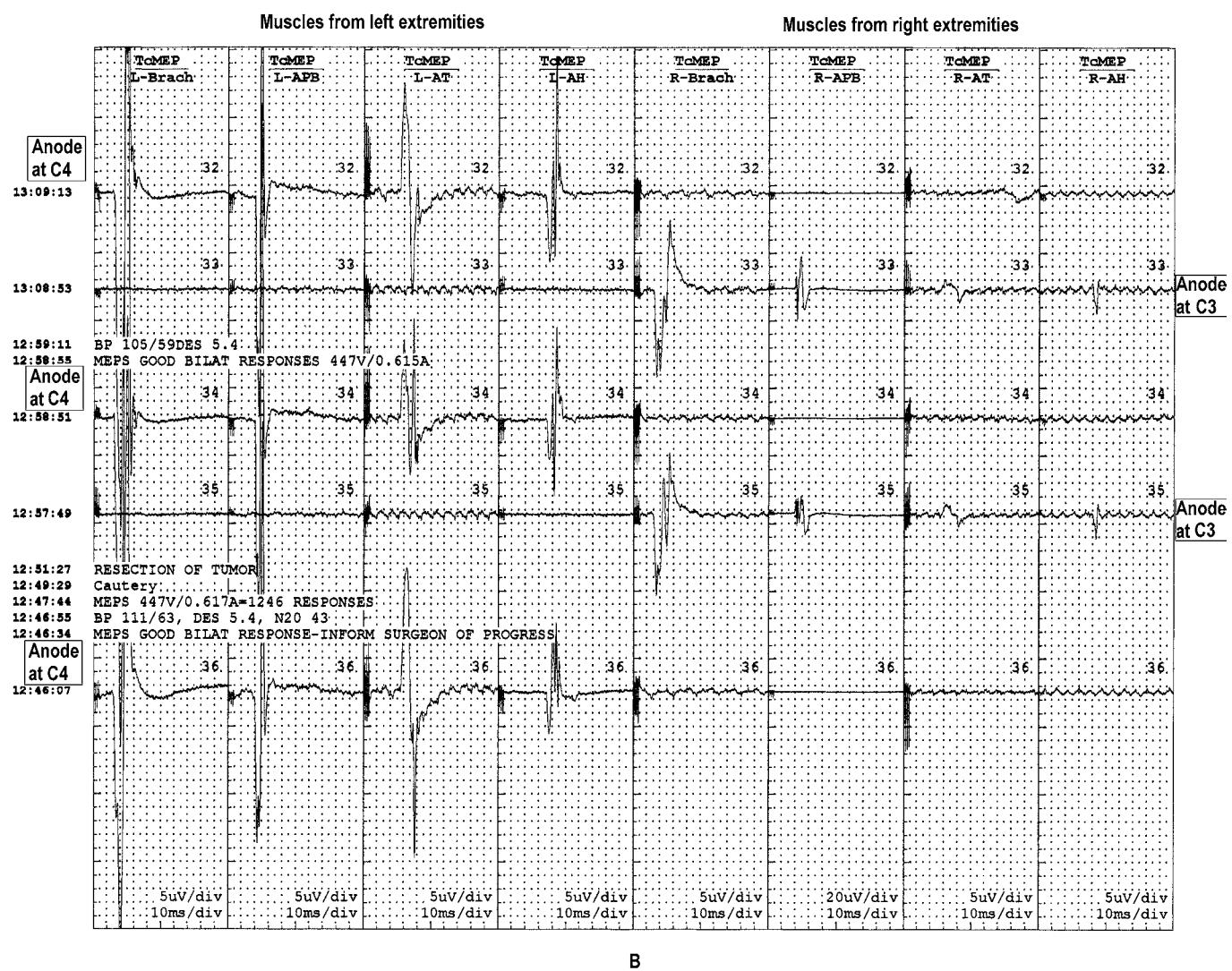
Figure 7-6. Cont'd.



**Figure 7-7.** An example of MEPs after transcranial electric stimulation with anode electrode at C3. MEPs appear bilaterally on both upper and lower extremities but predominantly over right extremities (anodal stimulation). (From Yamada T, Tucker M, Husain A. Spinal cord surgery. In: Husain AM, ed. *A Practical Approach to Neurophysiologic Intraoperative Monitoring*. New York, NY: Demos, 2008:117–137, chap. 8, with permission.)



**Figure 7-8. A-D.** This is a case of intraoperative TcMEP monitoring during intramedullary as well as extramedullary spinal cord tumor removal at T12-L2 spine. The well-defined MEPs were recorded from all four muscles (Brach, brachioradialis; APB, abductor pollicis brevis; AT, anterior tibialis; AH, abductor hallucis) bilaterally (**A,B**). (Note the MEPs were recorded from the extremities contralateral to the side of anode stimulation.) Shortly after removal of tumor, there was loss of MEPs from right lower extremity muscles at 13:25 (**C**). This was informed to surgeons at 13:27 after verifying the change (**D**). Lost MEPs did not recover at the end of surgery. Postoperatively, the patient had mild weakness of the right lower extremity.

**Figure 7-8. Cont'd.**

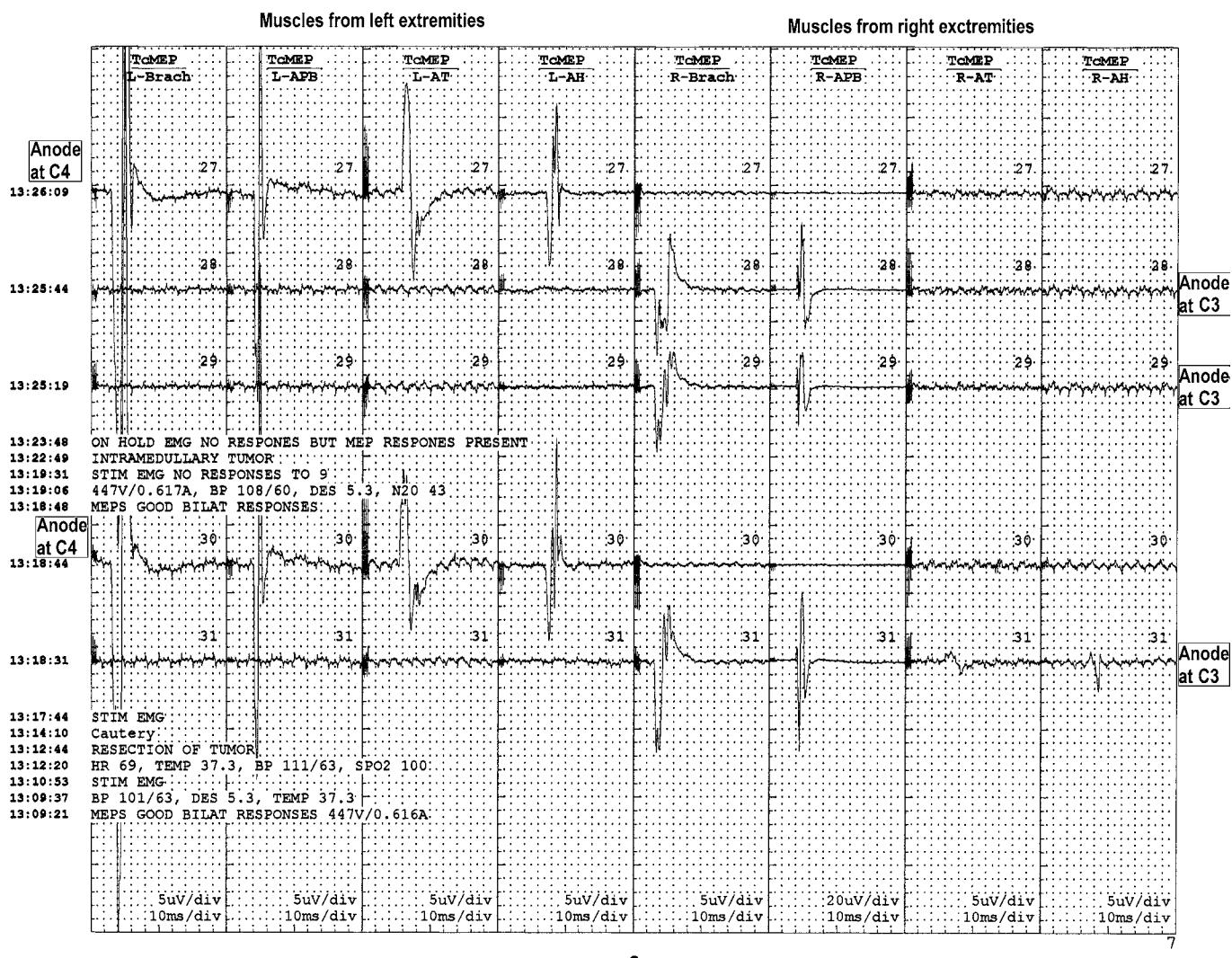


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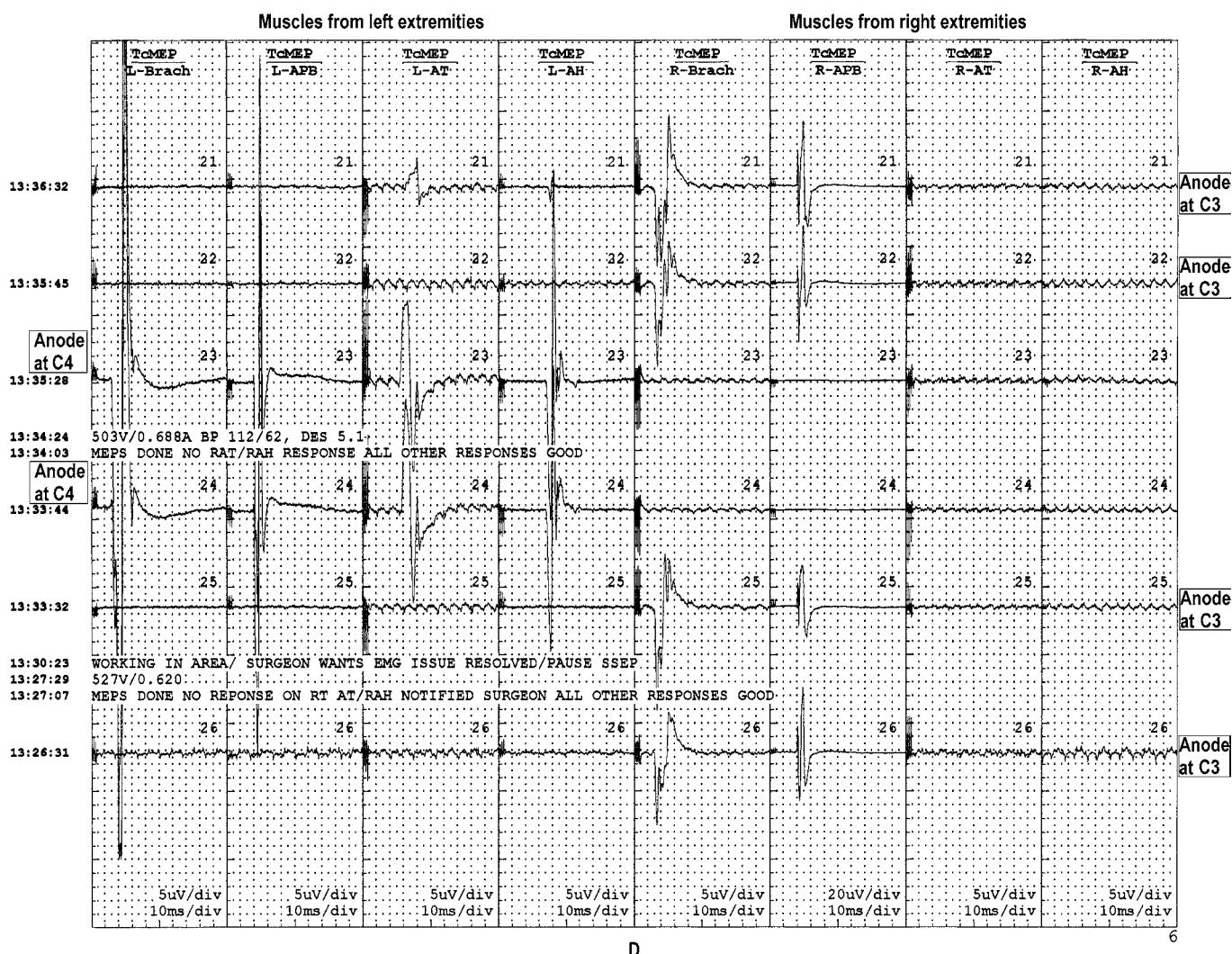


Figure 7-8. Cont'd.

## OTHER SPINAL CORD MONITORING METHODS

### RECORDING MEPs FROM THE EPIDURAL OR SUBDURAL SPACE AFTER TRANSCRANIAL ELECTRIC STIMULATIONS

For this type of monitoring, the recording electrodes are placed in the epidural or subdural space. These are flexible but semi-rigid wires with two electrodes exposed at the tip. These electrodes can be placed percutaneously in the caudal spinal cord through a Touhy needle catheter. In this approach, two catheter electrodes are placed: one rostral and the other caudal to the laminectomy in the epidural or subdural space. The response consists of a bi- or triphasic sharp discharge, called a D (direct) wave, followed by polyphasic waves, called I (indirect) waves (Fig. 7-9). The D wave results from direct stimulation of corticospinal neurons, whereas the I wave is generated by transsynaptic activation of corticospinal neurons. The D wave is resistant to inhalation anesthetics, in contrast to the I wave, which is extremely sensitive. The D wave can be elicited with a lower stimulus intensity than the I wave, and its latency becomes shorter with higher stimulus intensity. Generally, the stimulus intensity used is 400 to 600 mA or 400 to 500 V at 50- to 100- $\mu$ s duration.

### SPINAL CORD STIMULATION WITH RECORDING FROM SPINAL CORD, SCALP, MUSCLE OR PERIPHERAL NERVE

#### *Spinal Stimulation-Spinal Monitoring*

One can stimulate the spinal cord and record from the spinal cord at a distance from the point of stimulation. Disposable electrodes are used for this purpose. They are semirigid but flexible wires with electrodes exposed at the tip. They can be inserted through the ligamentum flavum after the spine is exposed and placed in the epidural space by the surgeon. By placing two sets of electrodes at the rostral and the caudal spine as either stimulating or recording electrodes, the spinal cord response can be recorded with a small stimulus intensity (usually <10 mA) (Fig. 7-10A,B; see also Fig. 7-12B). The response consists of NI and NII responses with

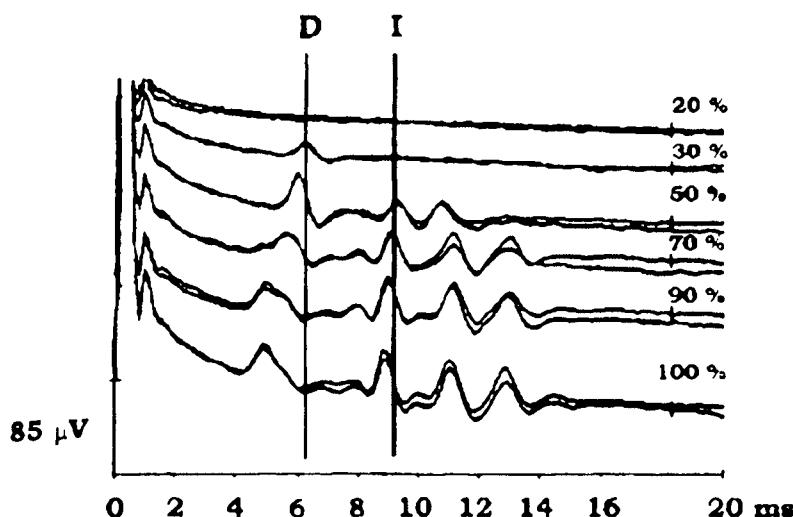
latencies less than 5 ms. NI and NII are thought to originate from the spinocerebellar tract and the dorsal column, respectively.<sup>28</sup>

#### *Spinal Stimulation-Cerebral Monitoring*

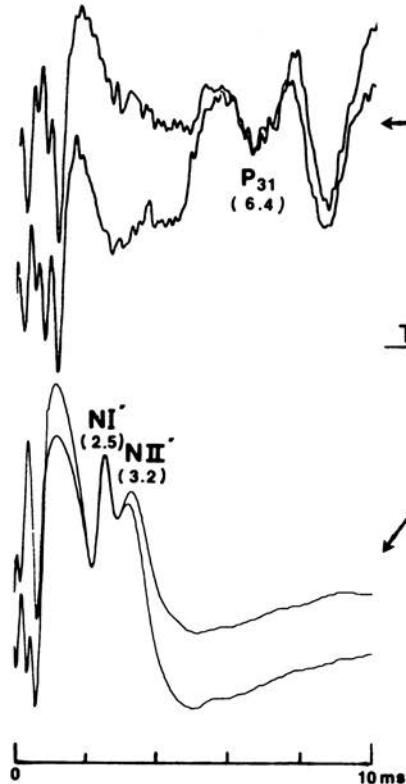
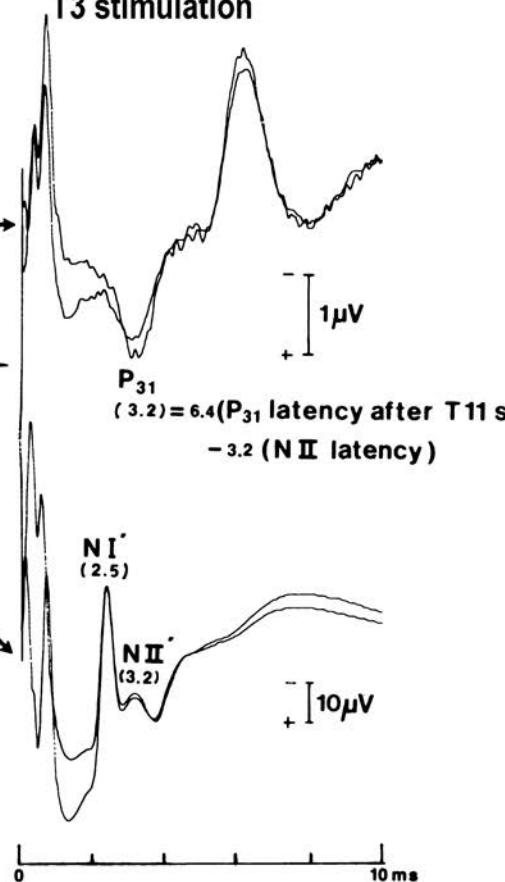
This method, though not used commonly, allows stimulation of the spinal cord and the recording of a cerebral response. This method reflects the integrity of the sensory pathway in the spinal cord, brainstem, and brain (Fig. 7-10A,B). This method of spinal cord stimulation with recording from spinal cord or scalp has some advantages: (i) it does not depend on peripheral nerve conduction and can be used in patients with a peripheral neuropathy or those whose peripheral nerve is not accessible, (ii) responses can be elicited by fewer averages in scalp recording or with no averaging in spinal cord recording, and (iii) responses are less influenced by anesthetic agents, especially for recording spinal cord responses. The main disadvantage of spinal cord stimulation is the insecurity of electrode placement. These electrodes can be easily dislodged during surgical maneuvers. Also, vigorous paraspinal muscle twitches in response to the stimulation may disturb the surgical procedure.

#### *Spinal Stimulation-Muscle or Peripheral Nerve Monitoring*

This method involves recording the CMAP from lower extremity muscles or action potentials from the peripheral nerve after spinal cord stimulation (Fig. 7-11). Both methods involve descending pathways, but it is not certain if they truly reflect motor pathways within the spinal cord. The latter method (recording the action potentials from peripheral nerves) was introduced as a neurogenic motor potential,<sup>29</sup> but later studies disputed this claim and have suggested that this is carried through dorsal column or primarily sensory pathways with minimal contribution from the motor pathway, if any.<sup>30,31</sup> Also, the recording of CMAPs from lower extremity muscles may not necessarily reflect the motor pathway in the spinal cord. Even if the anatomical pathway by this method is not certain or does not reflect the motor pathway, these methods can be utilized if the conventional monitoring methods are not possible.



**Figure 7-9.** Spinal cord responses (D and I waves) after transcranial electric stimulation. Note the D wave appears with weaker stimulation and progressively becomes larger and shorter in latency as the stimulus intensity increases (100% = 750 V). Polyphasic I waves follow D wave. (Reproduced from Deletis V, Shils J. *Neurophysiology in Neurosurgery. A Modern Intraoperative Approach*. New York, NY: Elsevier Science, 2002:38 (Chapter 2, Figure 2.7), with permission.)

**T11 stimulation****A****T3 stimulation****B**

**Figure 7-10.** Scalp and spinal cord responses after stimulation of the spinal cord at T11 (A) and T3 (B). After T11 stimulation, the scalp response showed expectedly longer latency of P31 (A) than that of T3 stimulation (B). The spinal potential consisted of two main negative components (NI and NII), which were recorded with the same latencies either by antidromic or orthodromic stimulation. (Reproduced from Machida M, Weinstein SL, Yamada T, et al. Spinal cord monitoring. Electrophysiological measures of sensory and motor function during spinal surgery. *Spine* 1985;10:407-413, with permission.)

**PERIPHERAL NERVE STIMULATION WITH SPINAL CORD RECORDING**

Alternatively, a rostral electrode can be placed in order to record a spinal cord response after peripheral nerve stimulation (Fig. 7-12A). These spinal responses consist of polyphasic waves that become more polyphasic at the more rostral recording site. This is in contrast to the much simplified wave form of the spinal cord potential (NI and NII) after spinal cord stimulation (Fig. 7-12B).

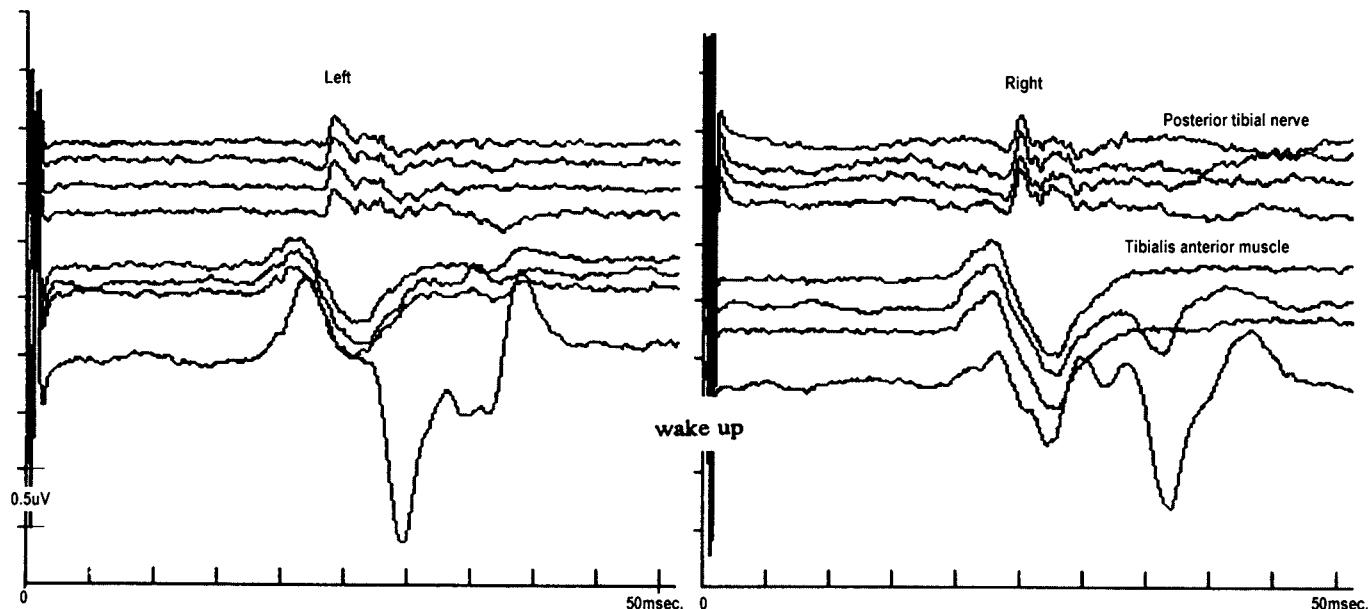
**ANESTHESIA DURING MEP AND SSEP MONITORING**

The appropriate choice of anesthetic agent will depend on the patient's underlying medical state, type and duration of the surgical procedure, and IOM modalities to be used. Both

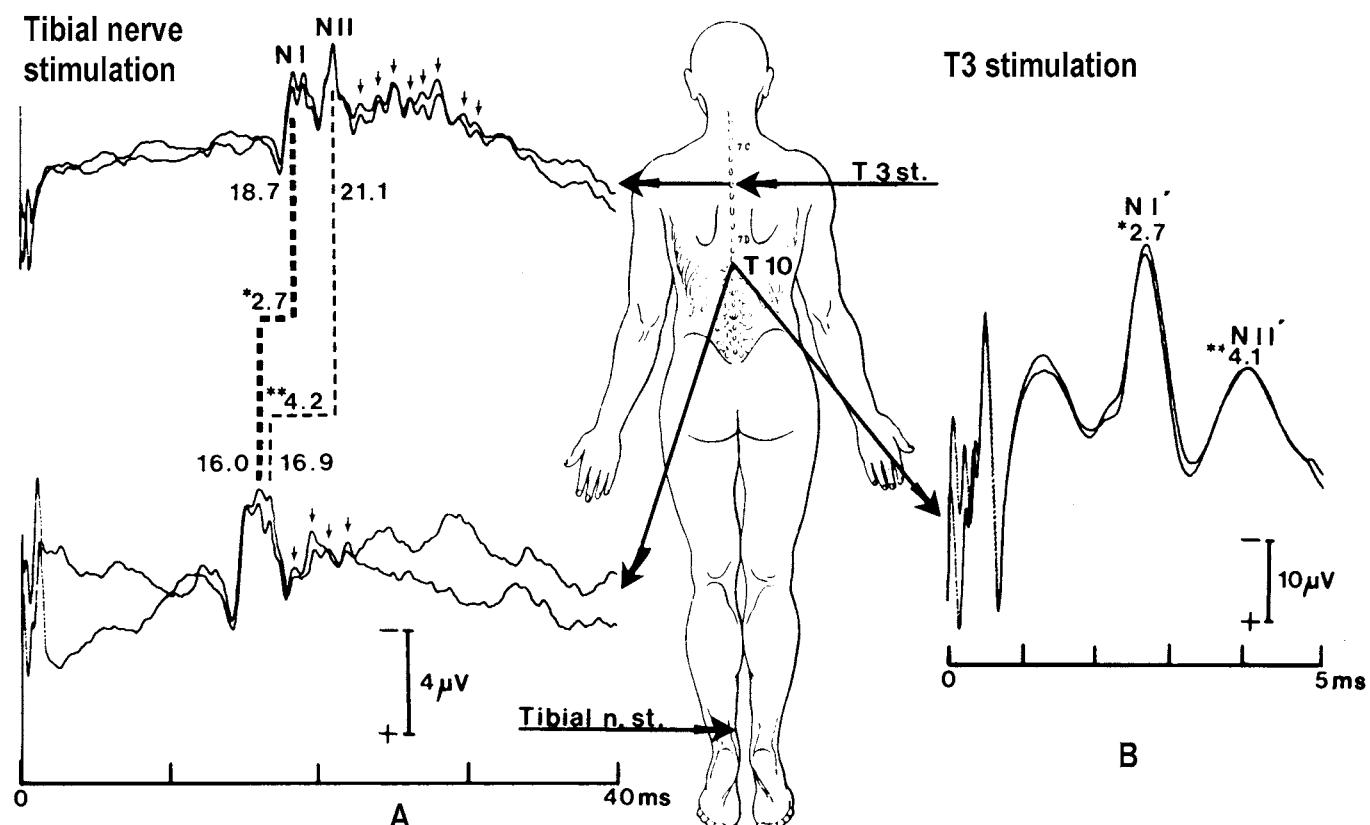
intravenous and halogenated anesthetic agents have their primary mode of action at the gamma amino butyric acid and N-methyl-D-aspartic acid receptors. These receptors mediate electrolyte channels that affect synaptic transmission involved in anesthesia.<sup>18</sup> SSEPs and MEPs are sensitive to the effects of inhalation anesthetic agents, particularly halogenated agents (isoflurane, sevoflurane, and desflurane) and nitrous oxide. Using these agents can significantly decrease the amplitude and prolong the latency of both SSEPs and MEPs and in some cases totally eliminate these evoked responses. MEPs are much more sensitive to inhalation anesthetics than SSEPs. In general, the chance of recording consistent and well-defined MEPs is much less with isoflurane greater than 0.5 or desflurane greater than 3.0.

These anesthetic effects are greatest on the cortical potentials, but over the course of surgery, these effects will be seen on the subcortical potentials as well. In contrast, with total intravenous anesthesia or TIVA, reliable SSEPs and MEPs can be

**Responses from muscles and peripheral nerves after spinal cord stimulation**



**Figure 7-11.** CMAPs are shown from the tibialis anterior muscles and peripheral action potentials from the tibial nerve at the ankle after stimulation of spinal cord. Both left and right CMAPs and peripheral nerve potentials were recorded simultaneously. (From Yamada T, Tucker M, Husain A. Spinal cord surgery. In: Husain AM, ed. *A Practical Approach to Neurophysiologic Intraoperative Monitoring*. New York, NY: Demos, 2008:117–137 (Chapter 8), with permission.)



**Figure 7-12.** Spinal responses after stimulations of peripheral nerve (A) and spinal cord (B). In contrast to the simplified waveform of spinal potential after spinal cord stimulation (B), spinal potentials after peripheral nerve stimulation were polyphasic more so with the higher spine level (A). (Reproduced from Machida M, Weinstein SL, Yamada T, et al. Spinal cord monitoring. Electrophysiological measures of sensory and motor function during spinal surgery. *Spine* 1985;10:407–413, with permission.)

obtained in the majority of patients. The most commonly used agent in this regard is propofol (Diprivan). Although it is sometimes argued that propofol carries a risk of patient recall for the surgical events under anesthesia, in actuality, less than 1% incidence of recall has been reported after propofol use.<sup>32</sup> Propofol is often used in combination with an opioid analgesic agent such as Sufentanil or Remifentanil to further lower the risk of anesthetic recall. When TIVA is not an acceptable choice, depending on the type of surgery or patient medical conditions, limiting the dosage of halogenated anesthetic to less than 0.5 MAC (MAC stands for mean alveolar concentration and is defined as the percentage of inhaled gas at which 50% of patients will not move after abdominal incision.) can allow reliable evoked potentials to be obtained in many patients.

It is important for the monitoring team to know the types, doses, and changes of anesthetic agents used during a case and to log this information in the monitoring record.

## EMG MONITORING FOR PEDICLE SCREW FIXATION

Transpedicular screw fixation may be used in the treatment of spinal deformity, degenerative disease, trauma, and tumors of the spine. Pedicle screws allow a more rigid fixation system than hooks and wires and allow the application of greater corrective forces to the instrumented spinal segments. From an anatomical viewpoint, as nerve roots exit the spinal canal, they tend to be aligned near the medial and inferior pedicle walls so that screws, which penetrate these walls, may cause nerve root irritation or injury (Fig. 7-13). Therefore, the ability to evaluate nerve root irritability after pedicle screw placement can lessen the risk of clinical radicular complaints postoperatively.<sup>33</sup> A CMAP is generated from the summation of many muscle fibers and is recorded using either surface or subdermal needle electrodes placed over the muscle belly. The muscles monitored are determined or planned based on the pedicle screw levels involved. Stimulating the pedicle screw while in the pedicle hole allows the detection of a possible medial or inferior wall breach that may not be detected by palpation by the surgeon or even fluoroscopically because of limitation of fluoroscopic views and patient anatomy.

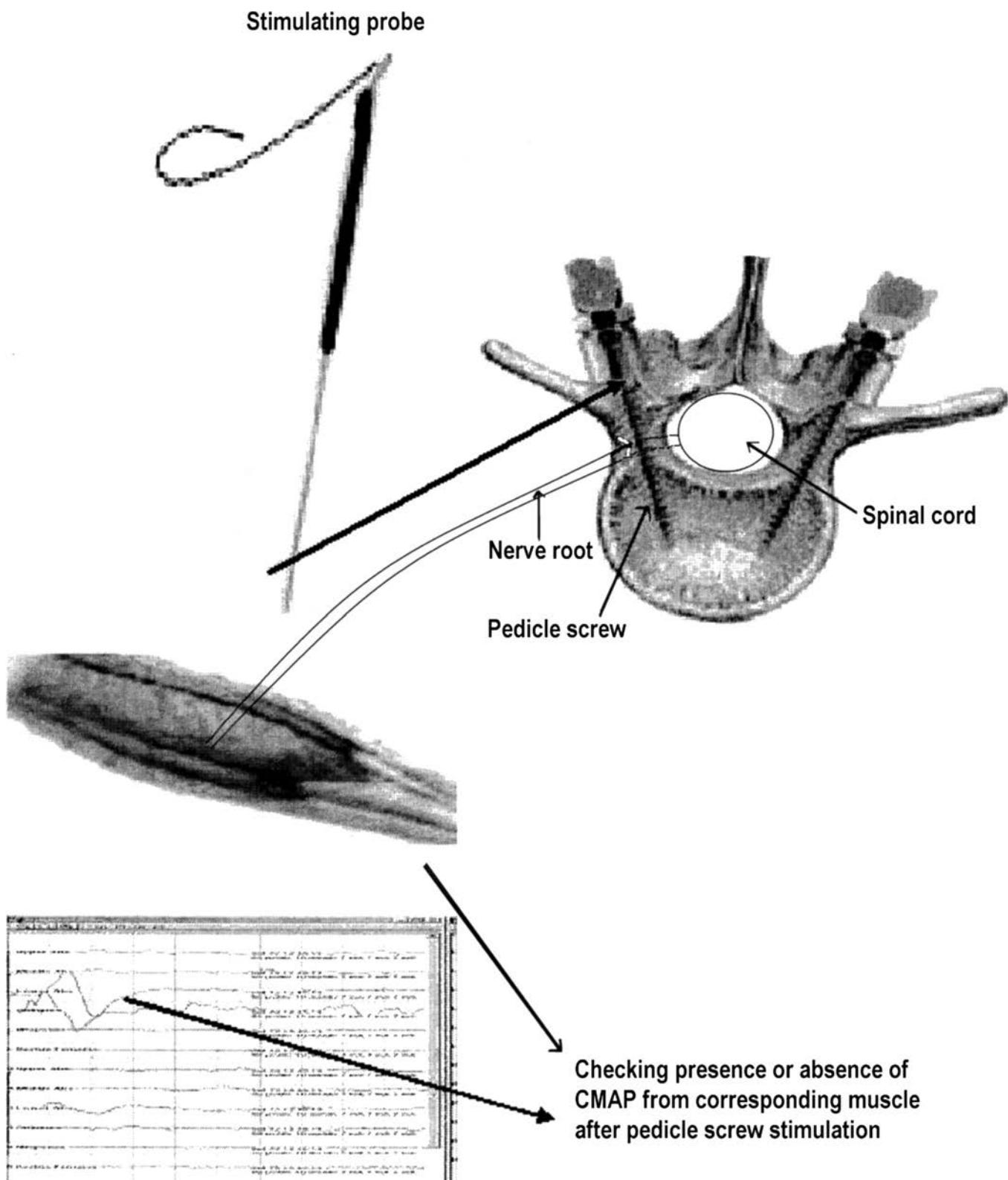
A wide bandpass filter of 30 Hz to 3 kHz is used to monitor the EMG activity. A free-run mode is used to evaluate spontaneous myogenic activity and the sweep is set at 1 s. Usually, there is minimal spontaneous activity (irritability) during the free-run recording. However, if there is preexisting nerve root irritation, low-amplitude spontaneous activity may be seen in bursts or frequent repetition, called "neurotonic discharges." Persistent neurotonic discharges indicate nerve root irritability or injury and warrant alerting the surgeon (Fig. 7-14). A free-run EMG recording allows assessment of irritability during pedicle screw placement, which can be reported to the surgeon. This may be difficult to interpret if there is a lot of noise from the Bovie (cautery) in the recording, and external interference should be minimized whenever possible. In order to assess screws in the thoracic level, rectus abdominus muscle obliques or intercostal recordings are made. Special care must be taken with intercostal recordings because of the inherent risk of lung or diaphragmatic perforation. Most often, information from the thoracic level can be obtained with recordings from the oblique and

abdominal muscles although, due to overlapping myotomes, assessment is over a range of levels rather than at a precise level. Figure 7-15 illustrates CMAPs recorded from the abdominal muscles during pedicle screw stimulation in the thoracic area. Subdermal needle electrodes or surface electrodes can be used for recording from these muscles with one needle in the belly of the muscle and the other needle 3 to 4 cm distal to it. For lumbar screw monitoring, muscle groups such as the vastus lateralis or medialis (L2-4) and tibialis anterior (L4-5) are helpful. After the surgeon has made the pedicle screw track (hole), a stimulating probe is inserted into each hole to test the integrity of the pedicle. Once the pedicle screw is placed, it is then stimulated, depending on the screw type either just under the head of the screw or at the top of the screw head for other screws. Blood and other fluids from the surgical field should be suctioned prior to stimulation as there is the potential for false-positive result due to the spread of current during stimulation. Conversely, dissipation of current may occur with the false-negative recordings.

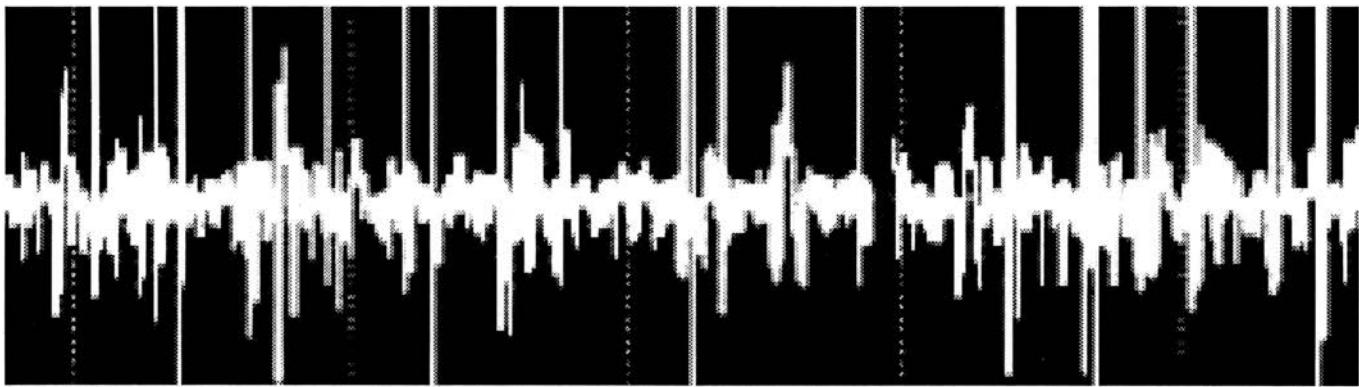
A CMAP elicited at or below a threshold level during pedicle screw stimulation may indicate the presence of a pedicle breach. Testing the track prior to pedicle screw placement and subsequent screw stimulation increases the accuracy of pedicle screw stimulation but also adds additional time to the procedure. If a CMAP is identified at or below threshold intensity, the pedicle is then carefully examined by the surgeon by palpation and a decision is made regarding shortening of the screw (unscrewed a few turns), a different screw utilized, or the screw eliminated altogether (if the screw is in a noncritical location). The threshold at which an alarm is raised is usually determined by experience with the procedure and the surgical staff involved or by using reproducible data on thresholds from institutions with similar experience in performing the procedure. Many centers will consider 6 to 8 mA threshold a significant level for alarm. In the lumbar spine, the threshold alarm level may be lower as the pedicles are larger. In some cases, pulling the screw out slightly, thereby effectively shortening it, and restimulating to see if a CMAP occurs can be done. Imaging with fluoroscopy can be useful as well to evaluate the pedicle wall and screw position. Surgical options may include the use of a shorter or thinner screw, shortening or turning out the existing screw, use of bone matrix or bone plug, or leaving the screw out altogether. Studies have been lacking in assessing the clinical follow-up of patients undergoing pedicle screw stimulation. These prospective studies would be useful to fully evaluate the sensitivity and value of pedicle screw monitoring in surgical spine cases.

## BRAINSTEM AUDITORY EVOKED POTENTIALS

Brainstem auditory evoked potential (BAEP) monitoring may be used for various cerebellopontine angle surgeries. These include microvascular decompression for hemifacial spasm (cranial nerve, CN VII), trigeminal (CN V) and glossopharyngeal neuralgia (CN IX), and acoustic neuroma (CN VIII). In trigeminal neuralgia, the patient complains of paroxysmal attack of pain over the face (in glossopharyngeal neuralgia the pain is in the throat) and also unilateral facial muscle twitching (hemifacial spasms) due to vascular compression of the cranial nerves at the level of root zone in the brainstem. These



**Figure 7-13.** Schematic model of pedicle screws stimulation in relationship to the nerve root. (The illustrated responses are the same as shown in Fig. 7-15.)



**Figure 7-14.** An example of neurotonic discharge indicating nerve injury or irritability.

conditions are often intractable to medical treatments. Because these cranial nerves are close to the vestibulocochlear nerve (auditory nerve or CN VIII) at the region of the cerebropontine angle, hearing loss due to injury to the CN VIII nerve is not uncommon. BAEP monitoring, in addition to the specific cranial nerve monitoring, is routinely applied for these surgeries. BAEP monitoring is also indicated for acoustic neuroma surgery that directly affects CN VIII.

Details of physiologic, anatomic, and pathological features and recording techniques are described in Chapter 3. Here only the relevant features of BAEP monitoring during these surgeries will be described.

Unlike SSEP and MEP monitoring, BAEP is much less sensitive to many anesthetics, either inhalation or intravenous. There may be slight latency prolongation (0.1–0.2 ms) without changes of interpeak latencies (IPLs) after anesthetic use, but this is not a problem as long as the control (baseline) response is obtained after anesthesia induction. BAEP is more sensitive to temperature or blood pressure change. For example, cold irrigation in the surgical field can cause prolongation of absolute latencies (without change of IPL) (Fig. 7-16). The wave V latency may prolong by 0.2 ms per 1°C temperature drop.

The stimulus used in the OR is the same as that used for routine clinical BAEP, consisting of broad band clicks and usually delivered through ear inserts. Headphones that are commonly used for routine BAEP recording in the laboratory are too large and interfere with the surgical field. It should be noted that the use of ear inserts causes absolute latencies to be about 1 ms longer than when using head phones due to the extra time inherent in sound traveling through the distance of the tube that connects the insert to the stimulator. The degree of delay is dependent on the tube length. Thus, the wave I latency is usually longer than 2 ms. The display window is 15 to 20 ms, which will cover the latency delay caused by using ear inserts and also the abnormal prolongation that may occur during surgery. The stimulus intensity is the same as for routine BAEP testing, that is, 70 dBSL. If hearing threshold is not tested preoperatively, increase the intensity until waves I and V are discernable.

The recording electrodes and montages are the same as used in routine clinical testing: Cz-A1 and Cz-A2 with a mid-frontal ground electrode. If wave I is not recordable even with the highest stimulus intensity, intraear canal electrodes or direct recording from the exposed vestibulocochlear nerve using wick or ring electrodes may be used.<sup>34</sup>

The band pass filter setting is 30 to 3,000 Hz (3 kHz), but the low frequency filter can be raised to 100 Hz and the high frequency filter can be decreased to 2 kHz, if necessary to reduce the various artifacts related to interference common in the operating room. A change in the filter will alter the latency and amplitude of waveforms, but this is irrelevant in a monitoring setting as long as the control (baseline) response is obtained with the same filter settings.

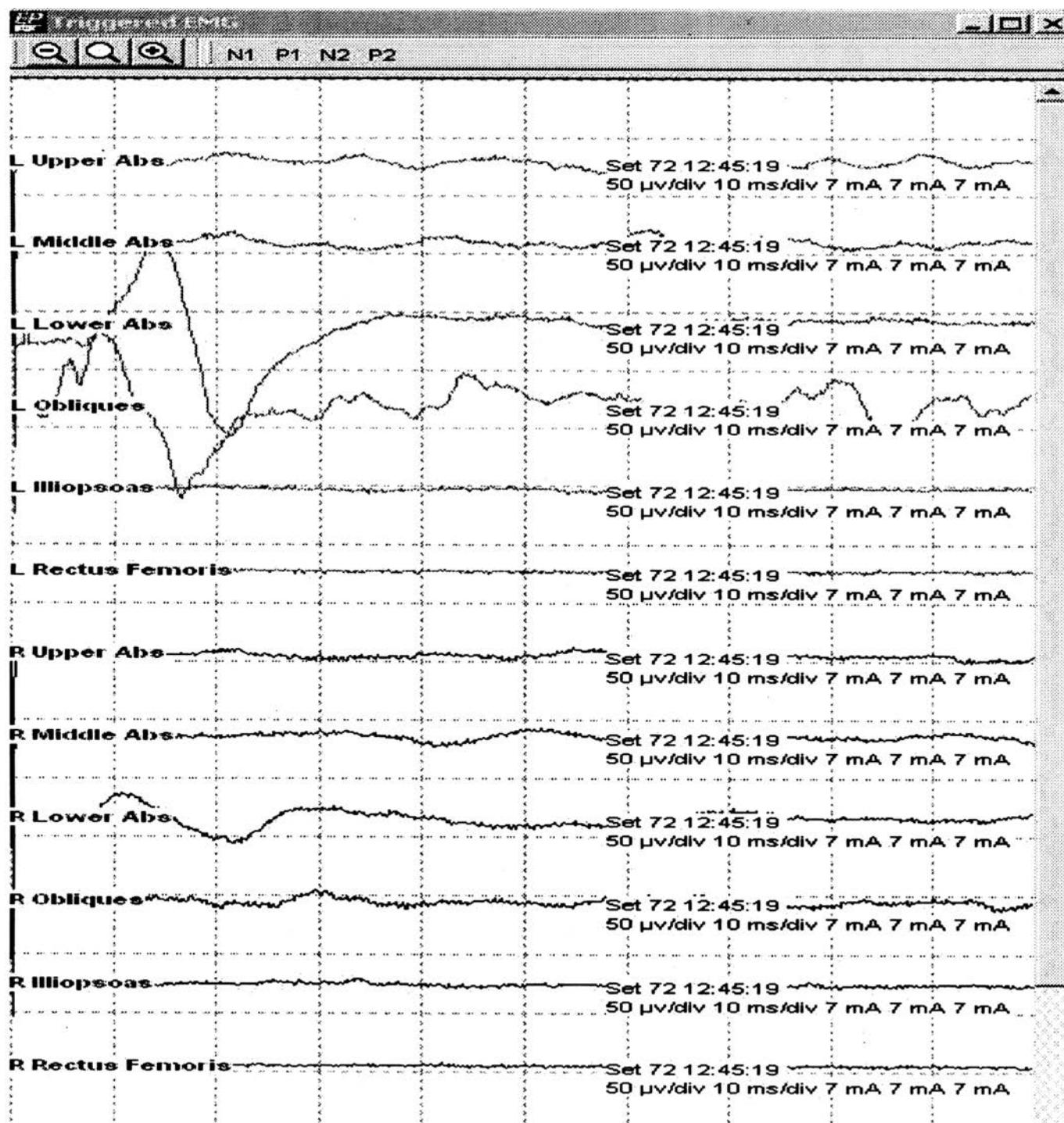
The stimulus rate can be faster than that used in a diagnostic BAEP, with rates of up to 20 to 30 Hz used. The faster stimulus rate slightly prolongs the latency and decreases the amplitude of the waveform, but this is also not a problem in the monitoring setting if the control response is obtained with the same stimulus rate. In fact, the faster stimulus rate is advantageous and preferred because it will yield the response faster than using a routine 10 to 11 Hz stimulus rate.

Of the various waves, wave V has the highest amplitude and is the most consistently recordable component; thus, “follow the V” is the primary target in BAEP monitoring. Because wave I directly reflects CN VIII nerve function, it is also important to monitor wave I. However, wave I is often small and may not be recorded, especially in patients who have a hearing deficit. If wave I identification is absolutely necessary, the use of intracranial electrodes or direct recording from vestibulocochlear (CN VIII) nerve may be necessary.

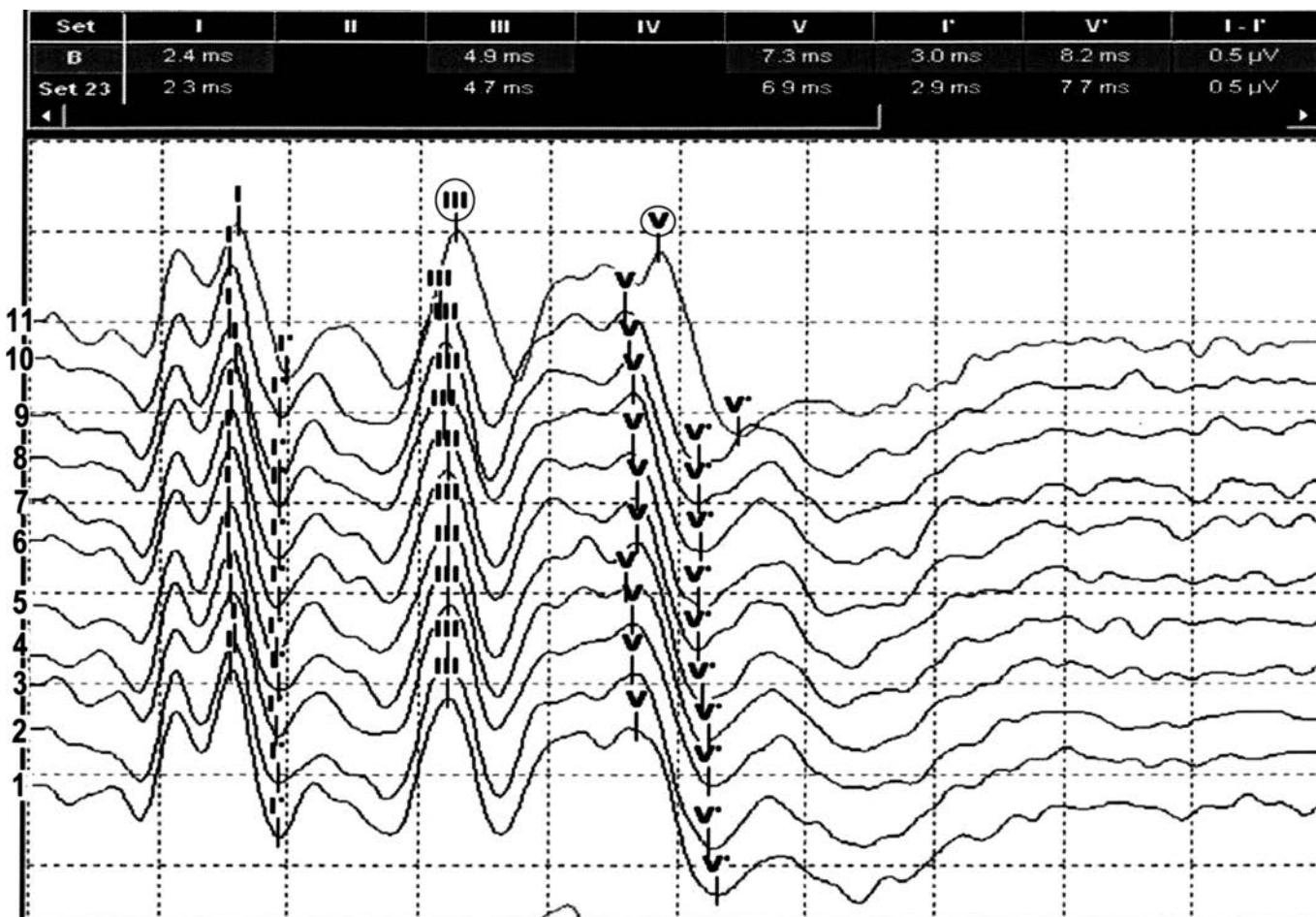
BAEP changes occur with mechanical stretches, compression, accidental transection of the nerve, or ischemia by impaired vascular supply to CN VIII.<sup>35</sup> Generally, a latency prolongation of 1 ms or an amplitude reduction greater than 50% of wave V baseline values is considered a warning sign for nerve damage.<sup>35</sup> A loss of wave I and subsequent waves indicates CN VII damage. If waves I and V are present but with prolonged IPL, impending intra-axial brainstem damage is suspected. At the end of the surgery, the presence of wave V usually indicates that hearing is preserved postoperatively, even if the latency is prolonged.<sup>36</sup>

## SUMMARY AND CONCLUSION

IOM allows for a safer surgical environment with less risk of neurological sequela when undertaken by a qualified NIOM team and when good communication occurs. This requires good coordination for the choice of modalities to utilize depending on the surgical procedure at hand and the ability to



**Figure 7-15.** An example of CMAPs from abdominal muscles during pedicle screw stimulation in the thoracic area. CMAPs were elicited by 7-mA current intensity from lower abdominal and oblique muscles. This suggested a pedicle breach was present, and the surgeons shortened the length of the screw inserted.



**Figure 7-16.** An example of BAEP monitoring. The responses were obtained every 2 minutes from No. 1 to No. 11. The responses were stable until No. 10 was recorded in which there was sudden prolongation of waves I through V (shown by circles) and No. 11 response had the greatest prolongation in wave V. This finding can be seen with excessive stretching of the nerve by a retractor, lowering temperature by cold irrigation, or a decrease in blood pressure.

evaluate the patient, both clinically and through neurophysiologic studies prior to the operative procedure. This coordination is best done by either direct physician involvement (depending on the surgical procedure) or continuous online real-time monitoring with ready access to the surgeon for discussion. Highly trained technical staff in the operative room is also vital to ensure the quality of the recordings, troubleshoot, and allow frequent communication with the monitoring physician regarding any neurophysiologic changes.

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## SECTION III

# Long-Term EEG Monitoring

CHAPTER

# 8

Erik K. St. Louis

## Diagnostic Video-EEG Monitoring for Epilepsy and Spells: Indications, Application, and Interpretation

### INTRODUCTION

Routine EEG sufficiently evaluates many patients with seizures or paroxysmal spells. Routine EEG can provide evidence for underlying diffuse or focal cerebral dysfunction through demonstration of background slowing or more distinct epileptiform abnormalities, which can support a clinical diagnosis of epilepsy in an appropriate clinical context. However, routine EEG also has limitations in both sensitivity and specificity; not all patients with epilepsy demonstrate interictal epileptiform discharges (IEDs, i.e., spikes or sharp wave activity), particularly in a single abbreviated laboratory study. Even worse, some patients without clinical seizures or epilepsy demonstrate epileptiform activity on interictal recordings, potentially misleading the clinician to commence antiepileptic drug (AED) therapy that may expose patients without actual clinical epileptic seizures to unwarranted and dangerous adverse effects.

Prolonged video-EEG monitoring rectifies these concerns in part by extending the recording period, thereby increasing opportunities to record diagnostically informative definitive

IEDs and allowing a safe environment for recording the patient's habitual clinical spells or seizure types under conditions of medication withdrawal or sleep deprivation. This chapter reviews appropriate video-EEG indications, discusses both outpatient and inpatient monitoring applications of video-EEG monitoring, offers practical pointers for interpretation of different spell and seizure types utilizing video-EEG technology, and concludes with a consideration of some pitfalls of this technique.

### APPROPRIATE SELECTION OF PATIENTS FOR MONITORING

Video-EEG monitoring is most appropriately reserved for the patient with an elusive spell or seizure diagnosis on clinical grounds who has sufficiently frequent episodes to permit capture during a scheduled timeframe of 1 week or less. In children and some adult patients who are having very frequent spells or seizures, at daily or near-daily frequency, video-EEG might yield an accurate diagnosis with planned admission for 2 to 3 days.<sup>1</sup>

Generally, spells or seizures should recur at least once or twice per month to enable capturing a spell during a planned 1-week admission, which has an approximate 75% diagnostic yield in our experience. Other recent studies have confirmed that video-EEG leads to altered diagnosis in 45% to 58% of patients and changes in management in nearly 75% of monitored patients.<sup>2,3</sup> However, video-EEG may still have a reasonable yield with less frequent spell occurrence. When seizures reliably occur during the menstrual period or another documented pattern of clustering, video-EEG can be planned during that expected timeframe. In patients with seizure episodes occurring rarely on drug therapy, seizures may still be successfully recorded during hospital admission for inpatient monitoring where AEDs can be safely lowered to permit seizure capture in a more abbreviated timeframe.

However, no specific seizure count should alone determine the utility of monitoring in patients with refractory epilepsy. The practice of video-EEG monitoring has evolved in parallel with the clinical practice of epilepsy care, the tenet of which is to assist a patient in becoming seizure-free, without adverse side effects of treatment, and when that may not be realistic or feasible, to reduce the frequency of medically and socially disabling seizure episodes to limit patient morbidity and improve quality of life. In keeping with this philosophy, video-EEG may be fairly applied to all patients with epilepsy in which one of these goals is not being met. When a patient is not seizure-free, he or she is at risk for injury and significant social morbidity, including inability to drive or to attend school or work to his or her full potential. One reason for suboptimal seizure control is inaccurate diagnosis of epilepsy or misdiagnosis of the patient's seizure type. Seizure recording enables an accurate diagnosis of the patient's seizure type to facilitate optimal drug therapy and provides an estimation of whether future epilepsy surgery or vagal nerve stimulator therapy is feasible. Not infrequently, an alternative diagnosis is established by video-EEG recording, such as psychogenic spells, for which AED therapy is ineffective. Patients with psychogenic spells who were mistakenly provisionally diagnosed with epilepsy can have that burden lifted, be reassured that their problem is not of an organic or physical nature, and subsequently be appropriately triaged to psychological and/or psychiatric care necessary to improve their condition.

On the other hand, not all epilepsy patients are candidates to undergo video-EEG monitoring. If a patient's diagnosis is clear on clinical grounds and empiric medications are successful in controlling seizures, video-EEG monitoring is not necessary in most cases.

## **INDICATIONS FOR VIDEO-EEG MONITORING**

### **SEIZURE/SPELL CLASSIFICATION**

When the diagnosis of epilepsy or the cause of paroxysmal spells is in doubt, ictal video-EEG recording of a patient's spell is the gold standard for establishing an accurate diagnosis.<sup>4</sup> Video-EEG should be considered for all patients who have an uncertain diagnosis of paroxysmal spells or episodic disorders. In certain patient groups such as the elderly, diagnosis of epilepsy can be difficult due to atypical seizure semiology and infrequent clinical episodes, and video-EEG might be particularly useful in clarifying a diagnosis of epilepsy.<sup>5,6</sup>

While epilepsy largely remains a clinical diagnosis made on the grounds of history obtained from the patient, clinical

features that are common to epilepsy and other paroxysmal disorders are often difficult to confidently distinguish by history taking alone. Patients may have incomplete recall of their seizures or difficulty describing their symptoms accurately. Clinical symptoms common to both seizures and nonepileptic spells such as syncope include prodromal warning symptoms, loss of consciousness, twitching movements, and even incontinence and injury. While seeking collateral history from observation of the spells or seizures by others is sometimes instructive and may clarify the diagnosis, such collateral history is frequently inaccurate, unreliable, or unavailable. Objective evidence through ictal video-EEG seizure recording can clarify the nature of a patient's spell from beginning to end, and permit intimate correlation of behavioral changes on video recording with underlying EEG activity, leading to an accurate seizure type diagnosis.

### **SEIZURE LOCALIZATION**

One third of those with epilepsy, approximately 750,000 individuals in the United States alone, suffer from refractory epilepsy. Epilepsy may be considered refractory to medication when two or more AEDs have failed to produce seizure freedom for a patient. Refractory epilepsy poses several risks to the patient, including impaired quality of life, morbidity from lost school or work attendance, injury, and even sudden death.<sup>7</sup> Epilepsy surgery is the single most effective nonpharmacologic therapy available for the treatment of refractory epilepsy, but patients must be very carefully selected for surgical treatment. Seizures must be partial in onset and begin exclusively from a single cortical region that is not critical for normal neurological functioning. Video-EEG monitoring and neuroimaging with a brain magnetic resonance image (MRI) are the crux of preoperative testing for surgical treatment for epilepsy. (Please refer to Chapter 9 for a thorough examination of the value of video-EEG monitoring in preoperative evaluation for epilepsy surgery, and other recent references on the subject<sup>8</sup>.)

### **SEIZURE FREQUENCY**

Even when the diagnosis of epilepsy and the patient's seizure type is well known, many patients underestimate the true frequency of their seizures. Determining the frequency of seizures is a central aspect of tailoring therapy for an individual patient. When patients or their caregivers are unable to provide an accurate estimation of seizure frequency, objective seizure quantification of a patient's current baseline seizure frequency with video-EEG monitoring may be an important step prior to instituting new medications or considering withdrawal of current treatments.

### **THERAPEUTIC ASSESSMENT AND TAILORING**

A related use of video-EEG monitoring is accurately quantifying the frequency of seizures in a patient with known severe epilepsy and daily refractory seizure episodes that are so brief in duration or subtle in character that they are difficult to fully characterize and count, making appropriately aggressive treatment difficult. Such a clinical situation is particularly frequent in newly diagnosed epilepsy, epilepsy with known clustering of seizures over a period of days, or acute symptomatic seizures related to catastrophic neurological disorders such as ischemic stroke, brain hemorrhage, or meningoencephalitis. In these instances,

seizure quantification with ictal video-EEG recording is often a vital adjunct to the clinician in determining the next appropriate step in treatment and offers a highly objective means of verifying the efficacy of newly applied medication trials.

## **APPLICATION**

### **OUTPATIENT MONITORING**

Several vendors now offer outpatient continuous EEG and/or video-EEG monitoring technology, enabling recording in the outpatient or even home environment. Potential advantages of a home monitoring approach include the opportunity to record in a more naturalistic environment to determine which seizure precipitants are involved, observation of the patient in his or her element of usual daily life, and avoiding significant disruption of the patient's obligations and lifestyle. Disadvantages of unsupervised home monitoring approaches include technical limitations such as electrode detachment and related artifacts, inability to optimally position recording cameras, inability to perform seizure-provoking techniques such as drug withdrawal, and lack of the educational and psychosocial support provided by an epilepsy center monitoring unit.<sup>9</sup>

Video positioning and electrode fidelity are key elements in a successful video-EEG recording. If patients happen to be off camera at the time of spell occurrence, behavioral correlate to the spell or seizure is lost. Furthermore, unless the recording is supervised closely by technologists and/or nursing personnel continuously, there is no opportunity to conduct response testing and ascertain whether a spell involves loss of awareness or consciousness. Electrodes frequently become dislodged in prolonged recording and require regular technologist monitoring and maintenance to preserve the fidelity of the prolonged recording. It is indeed frustrating for patients and their treating physicians, when at last the spell of interest is captured, but to find that the information obtained is nondiagnostic due to technical inadequacy of the recording itself.

For these reasons, home monitoring presents several technical challenges, and outpatient video-EEG conducted in a carefully observed clinic or hospital setting where response testing, attendance of the patient's comfort and needs, and optimization of all technical aspects of the recording is generally preferable. Outpatient video-EEG for limited durations of up to 8 hours for patients having daily spell or seizure occurrence is particularly convenient and has a relatively high yield. Patients with less frequently occurring seizures should generally be admitted to an inpatient hospital unit for a more prolonged period of observation and to withdraw seizure medications in a safe, supervised setting.

### **INPATIENT EPILEPSY MONITORING**

#### ***Unit Safety***

When establishing an inpatient epilepsy monitoring facility, several aspects of patient safety must be considered. First, location of the unit should be easily accessible to a well-staffed centralized nursing station that has continuous video surveillance of all monitored patients to permit instantaneous response to seizures when they occur. The room environment should be free of sharp edges on furniture and appliances to avert injury during potential falls, and when in bed, patient bed rails should be well padded and maintained in the upright position to prevent falls from bed.

#### ***Hiring and Training of Personnel***

Like any specialized hospital unit, specific personnel are central to the success of an inpatient epilepsy monitoring unit. Ideally, continuous EEG technologist monitoring of the recording best ensures patient safety, recording fidelity through replacement of faulty electrodes for optimal recordings, and response testing during clinical spells. Close and careful supervision by nursing staff with continuous availability of epilepsy physician oversight is necessary to ensure patient safety and to rapidly administer rescue drug therapies when patients experience prolonged seizures at risk for evolving into status epilepticus.

## **RECORDING EQUIPMENT AND TECHNICAL ASPECTS**

### **DIGITAL REFORMATTING**

The possibility to reformat previously acquired digital EEG data for optimal viewing by changing display sensitivity, filter applications, and montages has been a major advantage for seizure type determination and seizure localization. All modern commercial digital EEG systems offer this capability, and all epilepsy monitoring personnel should become familiar with special capabilities of their own equipment.

### **SEIZURE AND SPIKE DETECTION SOFTWARE**

Likewise, all currently marketed video-EEG vendors offer alternatives for efficient data review through computerized seizure and spike detection algorithms, each with their own strengths and weaknesses. The savvy EEG interpreter must realize that all such programs are flawed in one way or another, and that no system is perfect at accurately identifying all seizures, or excluding artifacts. Careful review of all interictal and ictal EEG recorded data is always necessary by EMU personnel, although computerized detection software techniques are useful for data reduction and in the selection of particularly suspicious interictal EEG segments for interpreting physician review.

## **CARE OF THE MONITORED PATIENT**

### **COUNSELING THE PATIENT PRIOR TO ADMISSION**

Patients should be informed that the goal of admission for video-EEG monitoring is to record one or more of their habitual clinical spells or seizures. Patients are frequently anxious about this suggestion since the act of drug withdrawal and a deliberate effort to record habitual seizures or spells seem counterintuitive; patients usually have understandable fear and anxiety about deliberately precipitating seizure episodes. Patients should be reassured that seizure recording is conducted in a safe setting with trained personnel capable of responding promptly to emergencies and that, in most cases, only a small number of recorded seizures is necessary to accurately diagnose their seizure type or localization. Patients and families are reassured by an advance tour of the epilepsy monitoring facility, so they will feel more comfortable with their planned admission. Patients often ask whether they should taper medications in advance of admission. Opinions differ on this practice and some insurers try to insist on preadmission medication withdrawal, but it is best and safest

to avoid tapering drugs until the patient has been admitted to the safety of the inpatient setting after intravenous access has been secured, enabling emergent drug administration to abort prolonged seizures if needed.

## **ADMISSION ORDERS**

Upon admission, at least one intravenous line should be placed in all patients for whom drug withdrawal is ordered, to enable rapid administration of rescue AED therapy if the patient should happen to develop a prolonged seizure or status epilepticus. Common rescue plans include administration of a short-acting benzodiazepine such as lorazepam 1 to 2 mg intravenously or administration of intravenous phenytoin or fosphenytoin at 20 mg/kg; if phenytoin or fosphenytoin are utilized, a slow infusion is necessary at rates at or below package insert guidelines to prevent hemodynamic compromise (i.e., hypotension, cardiac arrhythmia).

## **SEIZURE PRECAUTIONS**

Bedrails should be covered with either protective pads or taping to prevent patient injury. Bedrails should be kept upright at all times to prevent injurious falls. Nursing and monitoring technologist staff should be trained to respond rapidly to the bedside when a seizure occurs.

## **SEIZURE FIRST AID AND NURSING CARE**

Epilepsy monitoring personnel should respond immediately to the bedside when a seizure is recognized to prevent patients from falling from bed or being otherwise inadvertently injured. Tongue depressors and other foreign objects should not be inserted into the mouth as they may induce further oral trauma or, worse, become lodged in the airway. If the patient's convulsive movements are not particularly violent, positioning the patient on their side during or immediately after the seizure has ceased helps to prevent aspiration of secretions or postictal emesis. Postictal patients should not be abandoned until they are coherent enough to reliably remain in bed, as wandering or falls in the postictal state may also result in injury.

## **PERI-ICTAL PATIENT ASSESSMENT**

During a seizure, epilepsy monitoring personnel should observe any unusual posturing or movements that may not be fully visible on video, and narrate aloud during the ictus, describing what is being seen at the bedside. All patients should be assessed for level of consciousness by attempting to converse with the patient, and directed questions and commands to assess language and memory are helpful. To distinguish a simple partial seizure (where consciousness is preserved) from a complex partial seizure (when consciousness is impaired), a test phrase for ictal amnesia should be given. Use a memorable phrase you are unlikely to forget yourself, such as "Remember blue cherries," and repeat the command at least twice to ensure the patient is likely to hear it clearly, then, retest for memory of the phrase after a few minutes. Having the patient read a standard series of phrases (such as "Whiskey and water is a popular drink in Texas" and "They heard him speak on the radio last night") is especially helpful in lateralizing the side of a likely temporal

lobe seizure focus, since patients with a left temporal lobe seizure focus are typically unable to read a test phrase accurately in the postictal state for at least 1 minute or longer, whereas patients with nondominant right temporal lobe seizure foci most often read well in under 1 minute.<sup>10</sup> Assessing motor examination for pronator drift and the Babinski sign in the postictal state can occasionally be useful for seizure lateralization, although motor signs of Todd's paralysis (transient focal or unilateral weakness of limb after focal seizure) are often more variable and ambiguous.<sup>11</sup>

## **SEIZURE PROVOCATION**

### ***Antiepileptic Drug Withdrawal***

Whether or not AEDs are withdrawn is a highly individualized decision, depending on the clinical indication for monitoring and the patient's own seizure frequency, history, and current AED regimen. When withdrawing AEDs, one must ensure appropriate safety measures are in place, including seizure precautions and a specific rescue plan to readminister drugs rapidly and efficiently when the objectives for admission have been met or whenever a seizure cluster or status epilepticus occur. All patients having AEDs withdrawn should have an IV line in place for rapid administration of intravenous rescue medications. When discontinuing medications, it is generally advisable to cut each AED dosage into half each day until the patient is entirely off a particular drug. Certain medications with a particularly long half-life, such as zonisamide, or drugs that have novel mechanisms of action such as gabapentin, pregabalin, or levetriacetam, can in most instances simply be stopped upon admission. When restarting medications after several days discontinuation, restarting that patient's usual daily dosage is typical, although some medications can be rapidly reloaded, such as phenytoin or carbamazepine. Providing patients with a prescription for an oral, buccal, or rectal rapid-onset drug formulation for acute seizure treatment upon discharge is a wise precaution, especially following short hospital admissions involving rapid drug fluctuations, given a heightened risk of severe seizure clusters or status epilepticus following discharge.

### ***Sleep Deprivation***

Sleep deprivation is a reasonable provocative technique to attempt to increase the likelihood and efficiency of capturing seizure events. However, little evidence exists to support or guide the practice of sleep deprivation in epilepsy monitoring practice. One recent trial showed that a protocol of low-intensity sleep deprivation was of little value in increasing seizure yield.<sup>12</sup> However, different protocols of higher-intensity sleep deprivation, including all-night sleep deprivation, may still be effective in selected patients.

### ***Photic Stimulation and Other Techniques***

As in the outpatient EEG laboratory, photic stimulation (see *Practical Guide: EEG*, Figs. 9-6 and 9-7) and hyperventilation (see *Practical Guide: EEG*, Fig. 9-3) may also occasionally be employed to increase the yield of seizure and IED recording, particularly when primary idiopathic generalized epilepsy is suspected.<sup>13</sup> Patients with reflex epilepsies should also be tested with

whatever specific visual, somatosensory, or cognitive stimulus, which by history most regularly and reliably precipitates their seizures.<sup>14</sup> (see *Practical Guide: EEG*, Chapter 9). Protocols in the epilepsy-monitoring unit do not differ substantially from conventional lab techniques.

## EMERGENCIES IN EPILEPSY MONITORING UNIT PRACTICE

All patients admitted to an epilepsy monitoring unit (EMU) should have an individualized rescue plan in place for urgent or emergent medication administration in specific emergency situations, and for whenever the goals for that patient's admission to the EMU have been accomplished. All patients should also have a general rescue plan for prevention and treatment of status epilepticus. All patients having AEDs withdrawn should have an intravenous line in place for rapid readministration of rescue medications. One reasonable strategy is to utilize lorazepam 2 to 4 mg, at 2 mg/min, for a generalized tonic-clonic seizure of 5 minutes or longer duration, or if two consciousness-impaired seizures occur in rapid succession without an intervening recovery of consciousness. Some experts prefer to administer phenytoin or fosphenytoin at 10 to 20 mg/kg in this setting instead. Patients who are receiving benzodiazepines or phenytoin must have close respiratory, hemodynamic, and electrocardiogram monitoring during and following infusion to ensure patient safety.

If patients are elderly or hemodynamically unstable, an alternative is intravenous valproate 1,000 to 2,000 mg or levetiracetam 1,000 to 3,000 mg over 5 to 15 minutes (although providers should recognize that efficacy evidence for acute seizure treatment remains limited for both of these drugs).

If patients have continuing electrographic ictal activity despite administration of these first-line alternatives, they should be promptly transferred to an intensive care unit setting where high-dose benzodiazepine, phenytoin, and if necessary, barbiturate or anesthetic medications to terminate seizure activity can be safely administered, since intubation and mechanical ventilation are frequently necessary steps in such patients.

## INTERPRETATION

### INTERICTAL RECORDING

Video-EEG monitoring provides a rich opportunity to analyze prolonged samples of interictal EEG data, adding significantly to its diagnostic yield. Similar principles for review of interictal EEG (as outlined in detail in *Practical Guide: EEG*, Chapter 10) apply to epilepsy monitoring practice. The interpreting physicians should carefully review all interictal data for background slowing, which may be focal, regional, or generalized, as well as for the presence of IEDs. The type, localization, and frequency of IEDs are of significant diagnostic and prognostic value in diagnosis of the patient's specific epilepsy syndrome. For example, patients with mesial temporal lobe epilepsy who are being considered for possible epilepsy surgery having IEDs that are concordant to the surgical focus (i.e., unilateral anterior or midtemporal IEDs ipsilateral to the side of a surgical resection) have superior operative outcome to those who have other

discordant bilateral temporal or extratemporal IEDs.<sup>15</sup> Another example of the value of EEG in electroclinical epilepsy syndrome diagnosis is juvenile myoclonic epilepsy (JME) of Janz; of adolescent or adult patients having generalized IEDs on EEG who also meet clinical diagnostic criteria for JME, there is an approximate 80% to 90% chance of recurrent seizure activity following attempted AED withdrawal, so most clinicians favor lifelong treatment in such patients.<sup>16</sup>

Artifacts or benign variants in the EEG require careful distinction from genuine interictal abnormalities when interpreting video-EEG studies. An advantage of epilepsy monitoring practice is availability of continuous time-linked video so that patient movement and electrostatic artifacts can often be more readily distinguished and assigned a particular cause than in the laboratory. The reader is referred to *Practical Guide: EEG*, Chapter 13, which reviews appropriate recognition and interpretation of benign EEG variants commonly encountered in epilepsy monitoring practice, including mu activity, small sharp spikes, wicket waves, 14 and 6 positive spikes, and 6-Hz ("phantom") spike and wave (see *Practical Guide: EEG*, Chapter 13).

### ICTAL RECORDING

The main advantage of diagnostic video-EEG is the ability to intimately correlate clinical behavior simultaneously with EEG. Since either element may provide diagnostically useful data in specific spell or seizure types, both merit careful analysis.

### SPELL CLASSIFICATION: NONEPILEPTIC SPELLS

Nonepileptic spells are further subclassified into psychogenic or physiologic categories.

#### PSYCHOGENIC

Psychogenic nonepileptic spells (PNES) are common in epilepsy-monitoring unit practices, accounting for approximately 30% of admissions to epilepsy-monitoring units.<sup>17</sup> PNES are behavioral events that closely resemble epileptic seizures, but which lack the typical clinical and electrophysiologic features of true epileptic seizures. For this reason, it is appropriate to distinguish these events from actual seizure events by using the term psychogenic nonepileptic spells. While video-EEG telemetry is considered the gold standard for diagnosis, patients with PNES are less likely to have abnormal EEGs or MRI scans prior to admission and more often have prolonged spell duration, that is, often much longer than 1 minute.<sup>18</sup>

Typical features of PNES may be nearly identical to features of actual epileptic seizures, including behavioral unresponsiveness, abnormal movements, and postevent behavioral alteration ("postictal" behavior).<sup>19</sup> However, PNES are often distinguished by prominent, persistent eye closure throughout the spell (rarely seen in true epileptic seizures), usually have bizarre voluntary appearing movements including "yes-yes" type (head nodding) or "no-no" type (side-to-side head nodding) movements, prominent pelvic thrusting, or atypical progression of movements (e.g., clonic type movements that start in a leg, spread to the head, then back to an arm). Moreover, one PNES event is usually different from another, that is, individual PNES

lack stereotypy between different events. While PNES may very rarely be “triggered” by a preceding genuine epileptic seizure, the hallmark of PNES is the lack of an ictal epileptiform EEG discharge. However, extreme caution must be utilized and considerable experience is necessary to accurately diagnose PNES, since some true epileptic seizures lack EEG change and may have behavioral features that appear psychogenic.<sup>20</sup> Other pitfalls in the interpretation of PNES include EEG over-reading and movements that generate EEG artifacts that appear highly rhythmic or epileptiform.<sup>19</sup> Despite these difficulties in interpretation, PNES is usually accurately diagnosed within 2 days of admission to an appropriately experienced EMU.<sup>18</sup>

The usual cause for PNES is a psychological conversion disorder, where subconscious stress is being expressed in a physical way by the patient. Excellent communication is necessary between EMU personnel, patients, and their families. A compassionate, thorough explanation of the diagnosis and its distinction from true epilepsy is necessary to allow the patient’s insight into the diagnosis and eventually, possibly a full recovery. AEDs are not beneficial and only serve to expose the patient to needless adverse effects and risk, so once the diagnosis is secure, AEDs should be withdrawn unless they are being used for treatment of comorbid mood or highly suspected true epileptic disorders in addition to their diagnosis of PNES. Counseling and cognitive behavioral therapy are the most effective treatments, along with psychiatric care for associated underlying mood or anxiety disorders. Treatments are often only partially successful and relapses are frequent, sometimes requiring repeat diagnostic assessment.

## PHYSIOLOGIC

Physiologic nonepileptic spells may include neurologic or non-neurologic categories.

### *Neurologic*

Numerous paroxysmal neurologic disorders may be confused with epileptic seizures. These include nonepileptic behavior in cognitively impaired individuals, transient ischemic attacks (TIAs) from cerebrovascular disease, delirium, migrainous events, movement, and sleep disorders.

**NONEPILEPTIC SPELLS IN COGNITIVELY IMPAIRED INDIVIDUALS.** Cognitively impaired individuals are particularly likely to be misdiagnosed with epilepsy, or to have a mixture of nonepileptic behavior and true epilepsy.<sup>21</sup> Examples of nonepileptic behavior ascribed to epilepsy in this patient population include staring with unresponsiveness and movements mistaken for epileptic automatisms (i.e., stereotypes, voluntary mannerisms, or even tardive dyskinesia). When behavior that has presumed to have been epileptic on clinical grounds fails to respond to empiric AED treatment, video-EEG monitoring may help delineate epileptic from nonepileptic behavior.

**CEREBROVASCULAR DISORDERS.** Since the brain is heavily dependent upon oxidative metabolism, it requires a continuous supply of oxygen to function. The brain receives continuous delivery of oxygen from arterial vasculature. Cerebrovascular disorders may present with paroxysmal disturbances

of cerebral function, leading to diagnostic confusion with seizures. Cerebrovascular disorders result from cerebral ischemia (deprivation of blood flow and reduction of tissue oxygenation), or hemorrhage from rupture of a brain arterial structure. Ischemia is caused by either a thrombus, a blood clot forming in an arterial blood vessel that causes deprivation of blood flow to surrounding brain tissue, or an embolus, a fragment of thrombus from an upstream vascular segment that dislodges and travels downstream to an end arterial territory to lodge there and cause ischemia. Clinical characteristics depend on the duration of blood flow disruption and the arterial territory involved, and like seizures, a diversity of clinical symptoms may result. Short-lived ischemic attacks lasting only a few minutes produce fully reversible clinical TIAs, whereas ischemia lasting 30 to 60 minutes or longer generally produces some degree of irreversible, permanent cerebral damage and are termed strokes. Most commonly, cerebrovascular disorders cause loss of function (i.e., “negative symptoms”) such as numbness, weakness, visual loss, or aphasia, in distinction to epileptic seizures that almost always involve “positive” symptoms and signs during the ictal event (although postictal negative signs such as aphasia and weakness are common accompaniments of seizures, and loss of function with ictal weakness rarely occurs).<sup>22</sup> However, a gain of function including limb-shaking movements or symptomatic seizures from irritation of neighboring cerebral cortical tissue may occur, leading to diagnostic uncertainty in some cases. EEG is sometimes helpful in differentiating TIAs from seizures, since focal cerebral slowing or normal findings are seen on EEG during ischemic TIAs or stroke (typically polymorphic delta activity; see *Practical Guide: EEG*, Chapter 12, page 260), distinguished from focal evolving rhythmic activity accompanying most partial seizures.

**DELIRIUM/ENCEPHALOPATHY.** Delirium, also known as encephalopathy, is a reversible generalized confusional state induced by a systemic disorder. A diversity of different systemic conditions, including a toxin, alcohol or drugs, metabolic disturbance, hepatic or renal impairment, infection, or inflammation in the body may trigger delirium, and terms such as toxic-metabolic or septic encephalopathy are sometimes used when the cause is known. The hallmarks of delirium are disorientation and inattention, so that patients are unable to accurately name their current location or the date and are incapable of concentrating well enough to execute serial calculations or spell words backward. The clinical phenomena of confusion in a delirious state may closely resemble a complex partial or atypical absence seizure, involving blank staring with disorientation, inattention, and variable responsiveness, stupor with reduced vigilance, and unusual movements including myoclonic jerks. Encephalopathic patients may have acute symptomatic seizures, resulting in diagnostic confusion. EEG in a delirious patient may show either diffuse nonspecific nonepileptiform background slowing or even epileptiform-appearing patterns such as triphasic waveforms (see *Practical Guide: EEG*, Chapter 11).

**MIGRAINE.** The clinical phenomena of migraine and epilepsy are often similar, involving visual, sensory, and cognitive symptoms. Migrainous headaches often follow epileptic seizures, and cases of seizures following a primary migraine headache have also been rarely reported. However, in most patients, despite similar-sounding clinical stories, migraine and

epilepsy have distinctly different mechanisms. The EEG during a migraine attack demonstrates focal slowing, as opposed to partial seizures that may show focal evolving rhythmic activity (see *Practical Guide: EEG*, Fig. 12-17).

**MOVEMENT DISORDERS.** Some neurological movement disorders including paroxysmal dystonias and dyskinesias, and some tremor disorders, may resemble epileptic seizures. EEG is invariably normal during subcortically triggered movement disorders. Careful observation of the video clinical phenomenology by epilepsy and/or movement disorder specialists is necessary to distinguish these episodes since simple partial motor seizures may also demonstrate stereotyped movements lacking EEG change.

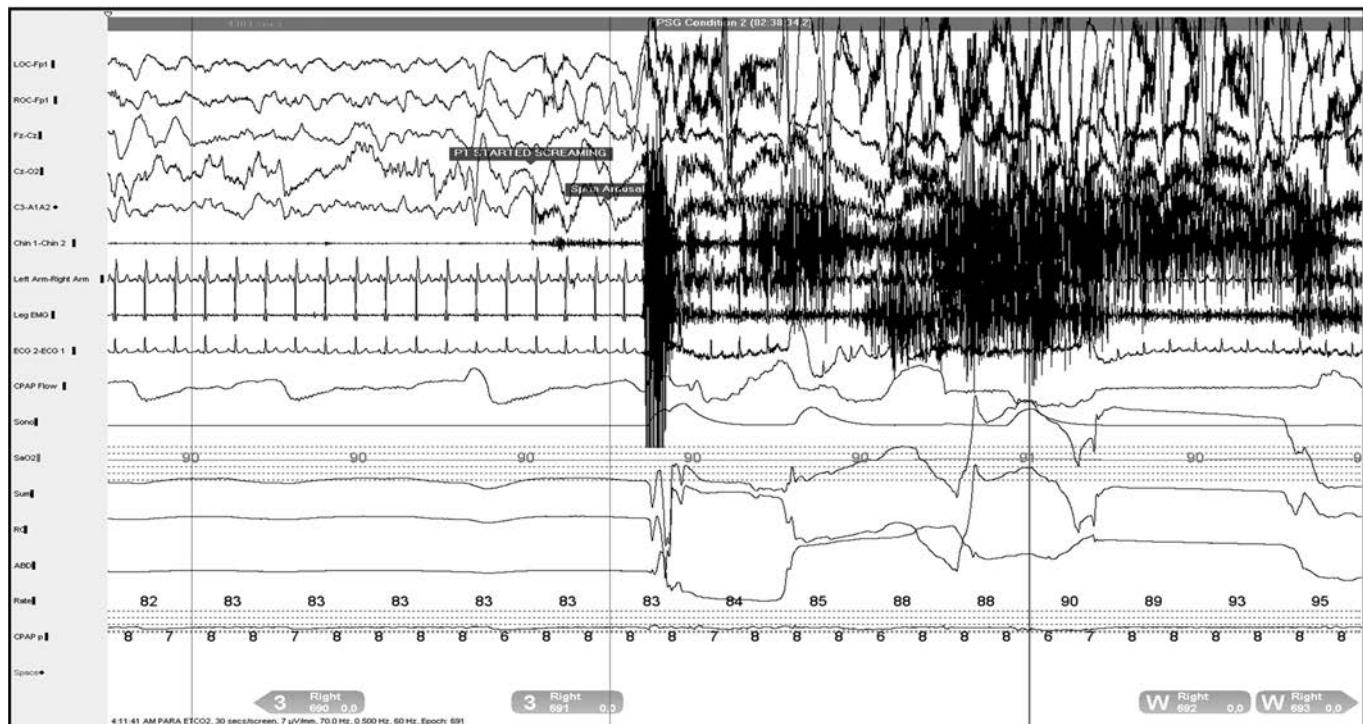
**SLEEP DISORDERS.** The two most common nocturnal events to be confused with sleep epilepsies are non-REM parasomnias or REM sleep behavior disorder. Nonstereotyped behavior on arousal, with or without vocalization, or sleepwalking behavior following, typifies NREM parasomnias. EEG may show no change other than arousal, but occasionally shows generalized or frontally dominant rhythmic delta or theta patterns lasting a few seconds following the arousal. Sleep terror (pavor nocturnus) or walking (somnambulism) typically appears abruptly from deep delta sleep without intervening arousal pattern (Fig. 8-1, see also Chapter 15, Figs. 15-4 to 15-6). REM sleep behavior disorder is characterized by complex motor behavior suggestive of dream enactment, with prominent vocalization and rapid phasic muscle jerks and heightened chin and limb muscle tone during REM sleep (Fig. 8-2; see also

Chapter 15, Fig. 15-7). In distinction, nocturnal seizures demonstrate highly stereotyped complex motor behavior, frequently with oral and/or limb or trunk automatisms. Seizures of temporal lobe origin show prominent focal evolving rhythmic activity, while frontal lobe seizures often show little if any ictal EEG change other than muscle and movement artifact, and diagnosis relies upon interpreter's experience and observation of stereotypy in such instances (see Figs. 15-12A,B, 15-13, and 15-14A,B).

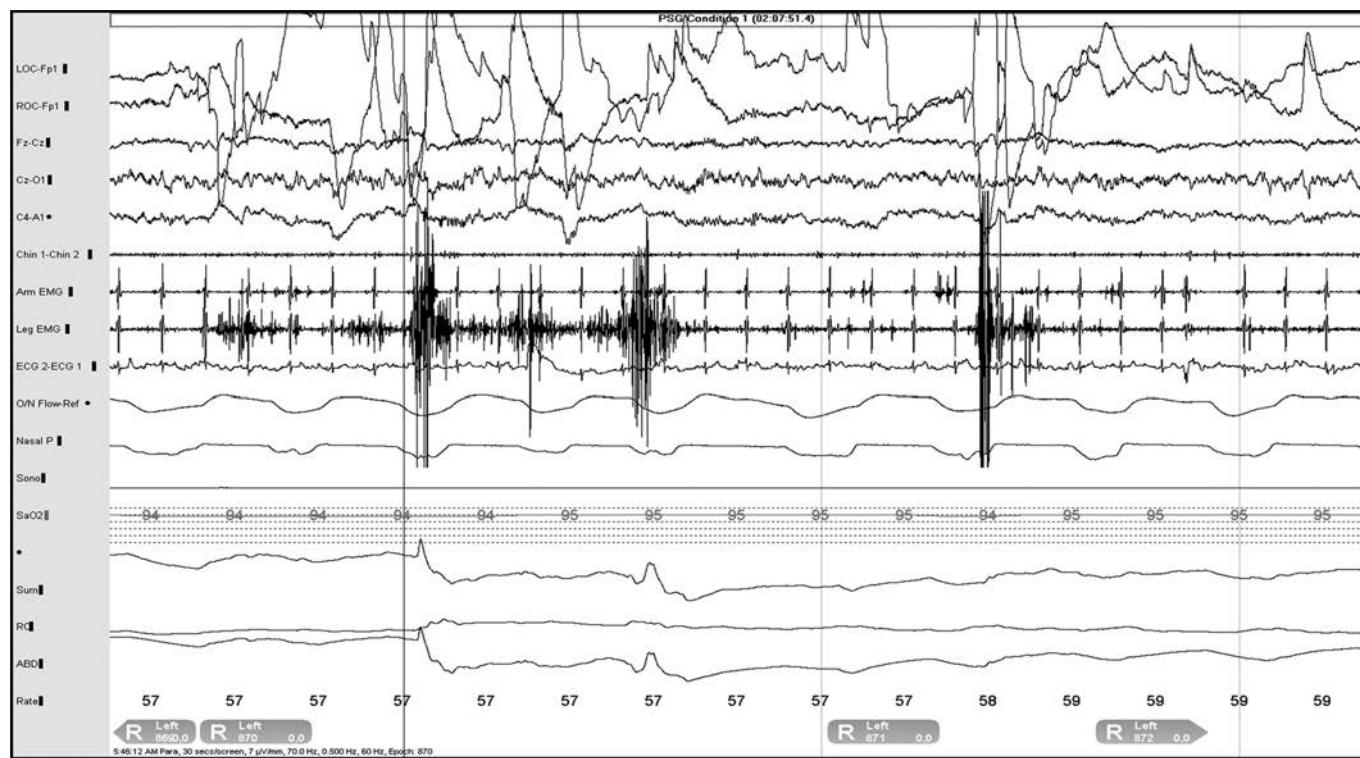
Cataplexy accompanying narcolepsy may occasionally be difficult to distinguish from astatic seizures. Diagnosis relies upon the historically reliable emotional provocation of cataplexy, especially following laughter or telling a joke (see Chapter 11, Fig. 11-5.). During a cataplectic attack, generalized alpha on EEG may be seen if the event is captured. Diagnosis can be made with confidence upon observing an episode and demonstrating reversible loss of knee muscle stretch reflexes during an attack, followed by recovery of reflexes in the interictal period.

### Non-neurologic

**SYNCOPE.** Syncopal disorders may result from either cardiogenic, vasovagal (so called simple faints), or hypotensive causes.<sup>23</sup> Vasovagal syncope is the most common and generally benign form of fainting, and is typified by a prolonged prodrome of lightheadedness, diaphoresis, and nausea, often following a positional change, physical exertion involving Valsalva maneuvers (lifting, toileting) or strong emotional circumstance (i.e., sight of blood, violence). Cardiogenic causes result from



**Figure 8-1.** Polysomnogram recorded during a typical NREM parasomnia, a confusional arousal. Note the abrupt arousal from N3 sleep, followed by partial obscuration by muscle and movement artifact with underlying high-voltage rhythmic delta activity. Corresponding clinical behavior of the patient was sudden arousal from sleep, sitting upright, and screaming. (Sensitivity: 7  $\mu$ V/mm, high frequency filter (HFF): 70 Hz, low frequency filter (LFF): 0.5 Hz, 30-second epoch).



**Figure 8-2.** A polysomnogram recorded during a typical episode of REM sleep behavior disorder. Note the underlying rapid eye movements, low chin EMG tone, and mixed-frequency EEG background activity typical of REM stage sleep, with significantly elevated transient muscle activity in the tibial EMG leads. Corresponding clinical manifestations were excessive phasic leg jerking, followed later by an episode of complex motor behavior consistent with dream enactment (Sensitivity: 7  $\mu$ V/mm, HFF: 70 Hz, LFF: 0.5 Hz, 30-second epoch shown).

cardiac brady- or tachyarrhythmias, and are less likely to have a prolonged prodrome of symptoms. Orthostatic hypotension, resulting from fall in blood pressure upon positional change, is a frequent cause of syncope in elderly and diabetic patients with autonomic neuropathy, and results in fainting following abrupt positional change from sitting to standing. EEG during each of these events shows generalized slowing or even suppression if blood flow is interrupted for a period of 20 to 30 seconds, such as during asystole following a particularly severe vasovagal attack (Fig. 8-3).

## SEIZURE CLASSIFICATION

Seizure classification is important in clinical practice, not only for a common nosology for describing information but also to determine appropriate therapy for an individual patient. Seizures are categorized according to defining clinical and electro-physiologic criteria set forth by the International League Against Epilepsy (Table 8-1).<sup>24-27</sup> Once the seizure type is known, other accompanying aspects of the clinical history can be factored in as well to permit assignment of an epilepsy syndrome diagnosis.<sup>25-28</sup>

Seizure behavior of disparate types and causes may closely resemble each other, requiring a rigorous, comprehensive assessment of both ictal semiology and ictal EEG characteristics to appropriately delineate competing possible diagnoses. For example, both absence and partial complex seizure types might involve similar behavior of staring, unresponsiveness, brief

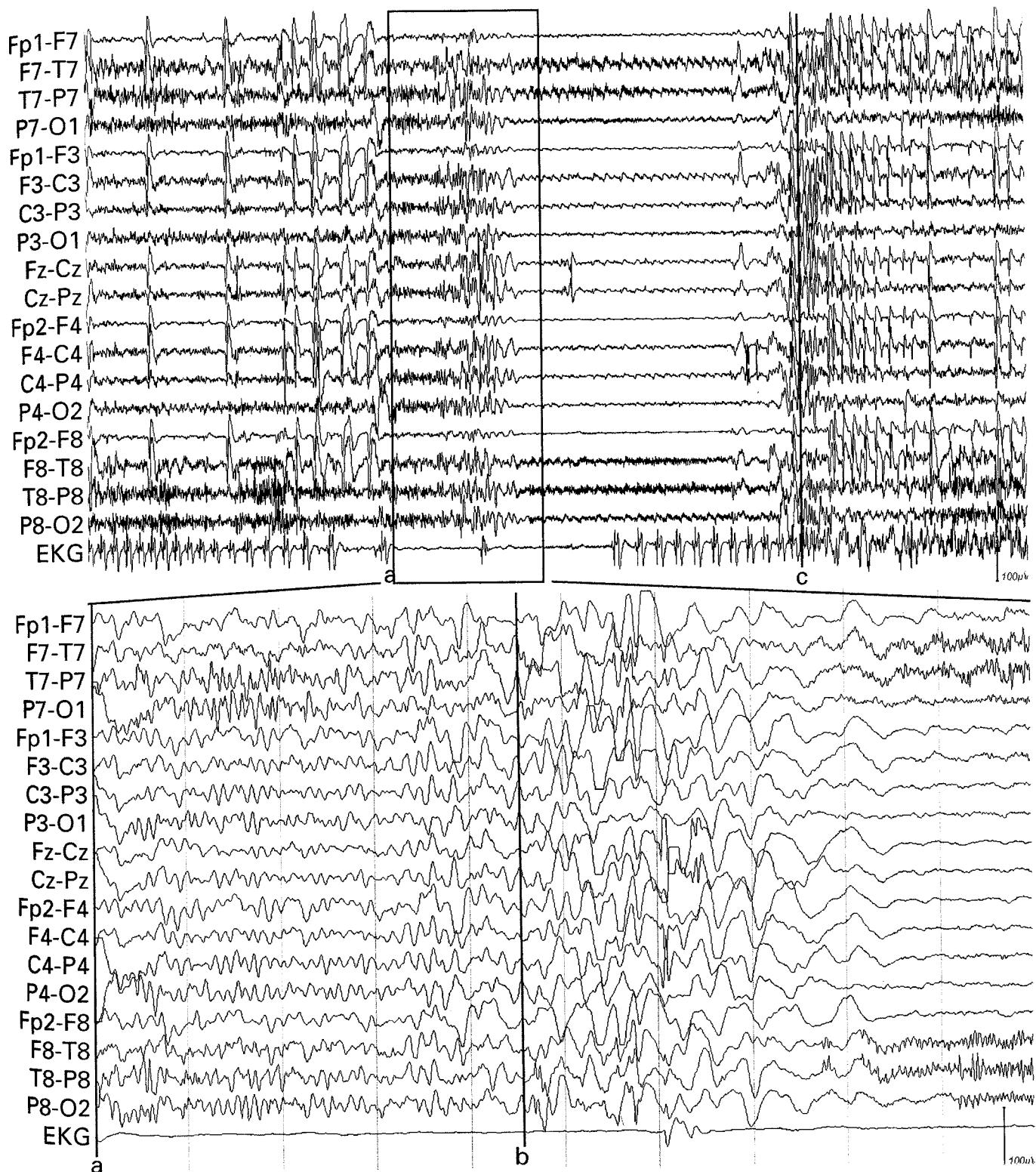
amnesia, and oral or manual automatisms. However, subtle differentiating clinical features such as a subjective aura and postictal behavior, specific types of lateralizing and localizing automatism or postures in the ictal behavioral semiology, and ictal EEG characteristics are usually very different and allow ready distinction between these two seizure types.<sup>29</sup> Patients with refractory partial-onset seizures might become candidates for surgery, whereas patients with absence seizures and underlying generalized epilepsy might be benefited by a change from narrow-spectrum AEDs (i.e., carbamazepine) that effectively

TABLE 8.1

Common Seizure Types as Specified by the International League Against Epilepsy

Partial	Generalized
Simple (consciousness preserved)	Absence
Complex (altered or lost consciousness)	Myoclonic
Secondary Generalized Tonic-Clonic	Clonic
	Tonic
	Atonic/astatic
	Tonic-clonic

Source: ILAE: Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia* 1981;30(4):389-399.



**Figure 8-3.** EEG recorded during a syncopal episode. Note diffuse delta slowing associated with bradycardia and asystole in EKG channel. EEG of block section corresponds with the EEG of lower figure. (From Quigg M, Bleck TP. Syncope. In: *Epilepsy: A Comprehensive Textbook*. vol. 3. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2008; 2701; Figure 1, with permission.)

treat only partial seizures, to a broad-spectrum drug that treats varying generalized seizure types equally well, such as lamotrigine or valproate.

### PRIMARY GENERALIZED SEIZURES

Primary generalized seizures result from bisynchronous cortical seizure onset and are reflected by a narrow and well-defined group of possible seizure behaviors and electroencephalographic patterns.

#### *Absence*

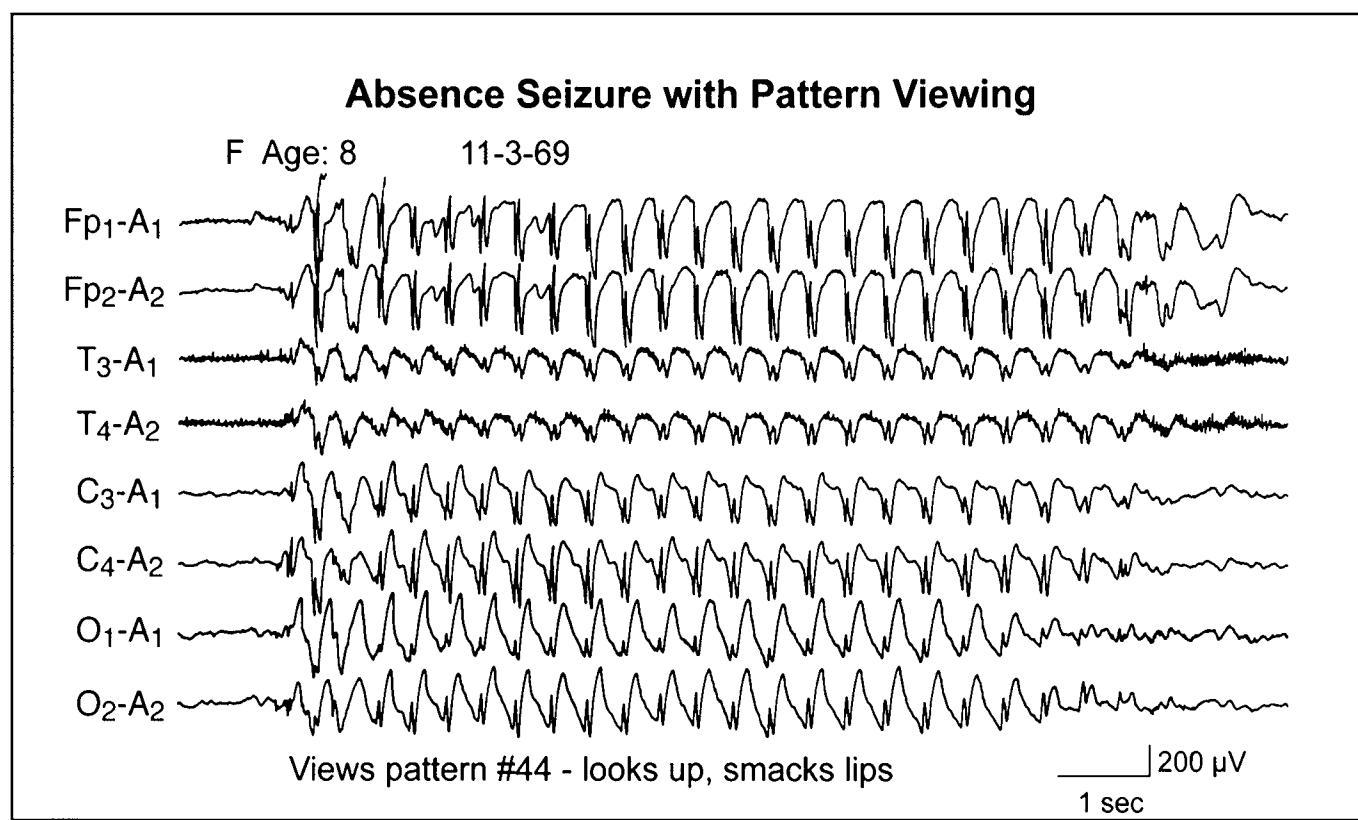
Absence seizures involve consciousness disturbance for 5 to 10 seconds, with or without accompanying automatisms, and lack a prodromal aura or postictal state. The behavior may closely resemble that of a complex partial seizure, or daydreaming behavior in a school age child. Attacks may be readily precipitated by hyperventilation (see *Practical Guide: EEG*, Fig. 9-3) or occasionally by photic stimulation or viewing of high-contrast visual patterns (see *Practical Guide: EEG*, Fig. 10-13). Absence seizures are most common, and often the exclusive seizure type seen in childhood absence epilepsy (CAE), the chief primary idiopathic generalized epilepsy syndrome of childhood with onset in the first decade of life.<sup>30,31</sup> CAE most often remits by the mid-teenage years. Ictal EEG shows generalized 3-Hz spike and wave activity (Fig. 8-4).

#### *Atonic/Astatic*

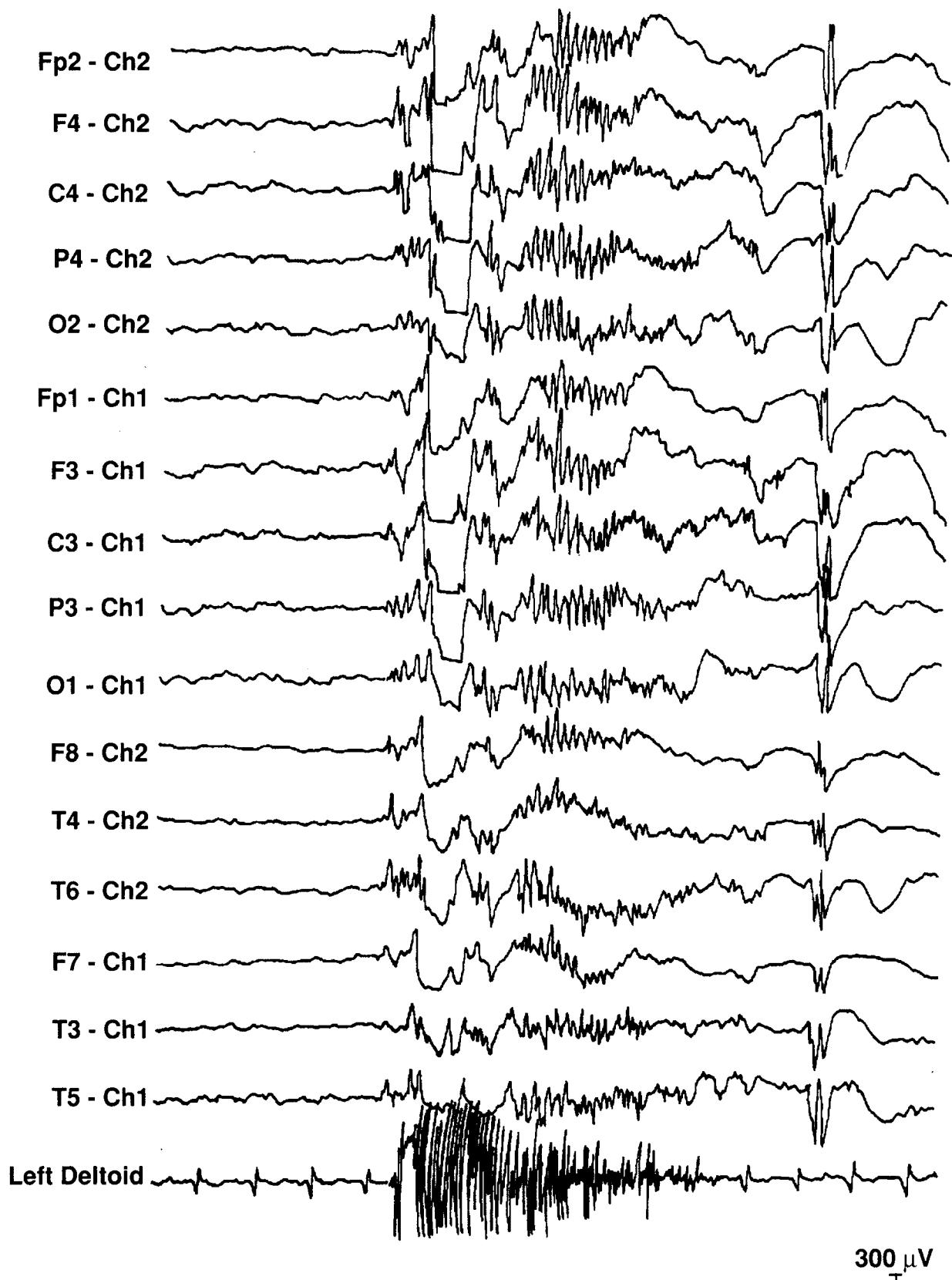
Atonic/astatic seizures are characterized by a sudden loss of postural tone, with variable severity from head nods/drops to complete loss of axial posture with falling and injury. Atonic/astatic seizures frequently occur in children with Lennox-Gastaut syndrome or another form of symptomatic generalized epilepsy, but they can have their onset in later life following generalized cerebral hypoxia. Attacks are often refractory to medical therapy, so that ambulatory patients may require prescription of a protective "crash" helmet. EEG shows polyspike-wave (Fig. 8-5; see also *Practical Guide: EEG*, Fig. 10-23) or an electrodecremental pattern with generalized fast activity (see *Practical Guide: EEG*, Fig. 10-28).

#### *Myoclonic and Clonic*

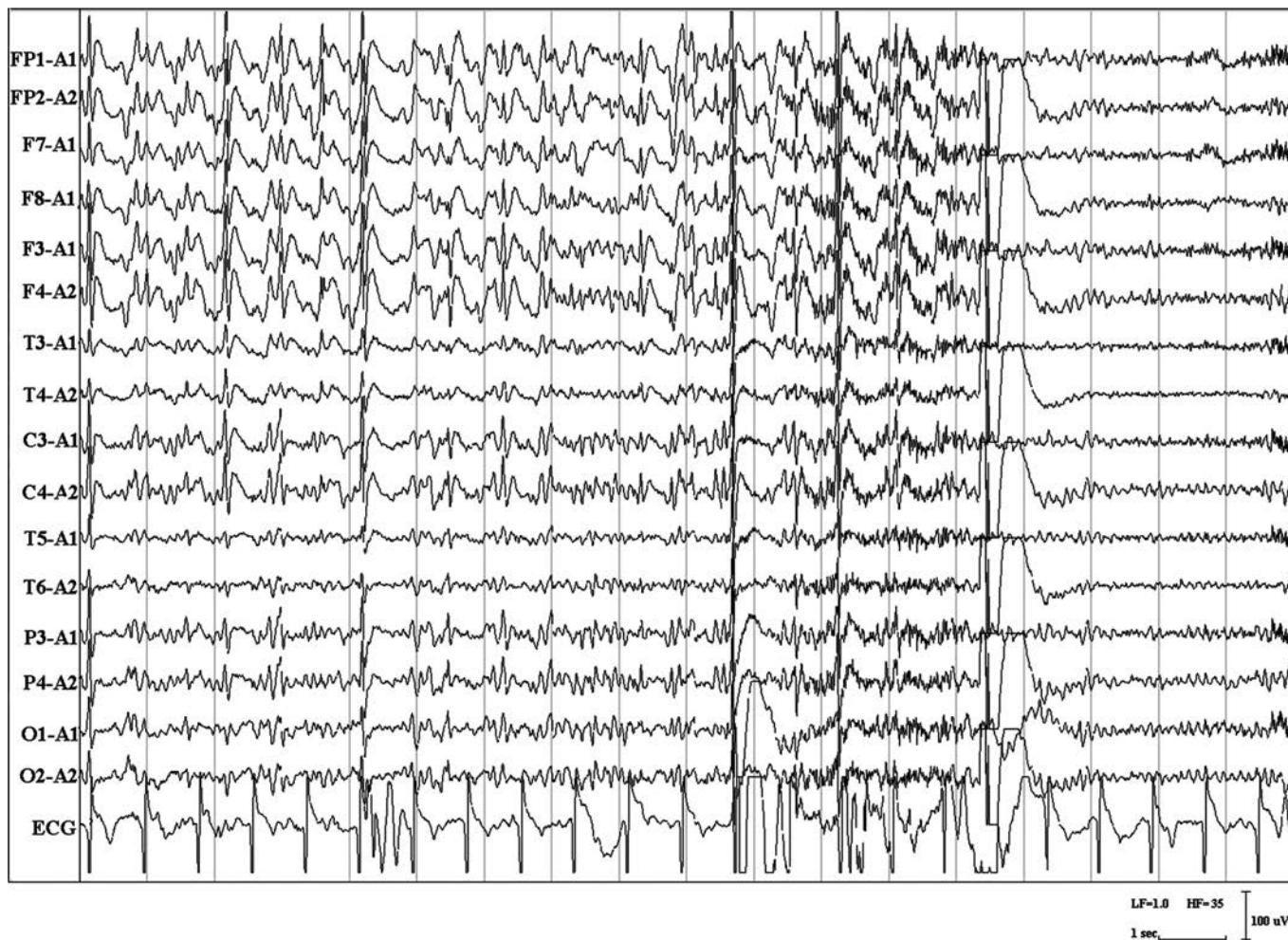
Myoclonic seizures involve sudden brief jerks or twitching of any limb or axial musculature, usually with preserved consciousness. Repetitive myoclonic seizures may merge and escalate into sustained generalized clonic seizures (essentially, a bisynchronous bodily convulsion without any preceding tonic phase). Massive myoclonus involving the trunk may lead to falls and injury. Myoclonic seizures are especially frequent in patients with adolescent-onset primary idiopathic generalized epilepsy syndromes such as JME.<sup>30</sup> Ictal EEG patterns include generalized spike and wave or polyspikes (Fig. 8-6; see also *Practical Guide: EEG*, Figs. 10-22 and 10-23).



**Figure 8-4.** An absence seizure is provoked by viewing of a provocative visual pattern. The EEG waking background is suddenly disrupted by generalized 3-Hz spike-wave activity at seizure onset. Clinical manifestations of the seizure were behavioral arrest, staring, momentary unresponsiveness, and mild oral automatisms. (Sensitivity: 5  $\mu$ V/mm, HFF: 70 Hz, LFF: 1.0 Hz, 12-second epoch).



**Figure 8-5.** An astatic seizure. The EEG waking background is abnormally slow, with slow-spike wave activity with a repetition rate of approximately 2 Hz. Note the muscle artifact on polygraphic recording depicting a component of tonic contraction with 15-Hz activity during video-electroencephalography. (From Tatum WO IV, Farrell K. Atypical absence, myoclonic, tonic, and atonic seizures. In: Wyllie E, et al. eds. *The Treatment of Epilepsy: Principles and Practice*, 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006, with permission.)



**Figure 8-6.** Myoclonic seizure. The EEG waking background is normal, with frequent admixed generalized spike-wave discharges. Seizure onset is shown in second 14 in the last quarter of the page, manifested by a spike-wave complex followed by brief generalized background attenuation. The clinical accompaniment was a sudden single jerk of both upper extremities. (Sensitivity: 5  $\mu$ V/mm, HFF: 70 Hz, LFF: 1.0 Hz, 18-second epoch).

### Tonic

Tonic seizures feature generalized tonic stiffening caused by co-contraction of agonist and antagonist musculature. Typical seizure semiology involves abduction of the upper extremities with extension of the legs, with the patient holding this “cross-like” posture for several seconds. Sleep is an activating influence. Although most tonic seizures are brief and less than 15 seconds in duration, escalation into tonic status epilepticus with prominent autonomic instability may occur. Vocalization, apnea, and falling may occur. Tonic seizures occur as part of the rubric of seizures in symptomatic generalized epilepsies such as the Lennox-Gastaut syndrome. Ictal EEG demonstrates generalized polyspikes, often obscured by muscle and movement artifact (Fig. 8-7).

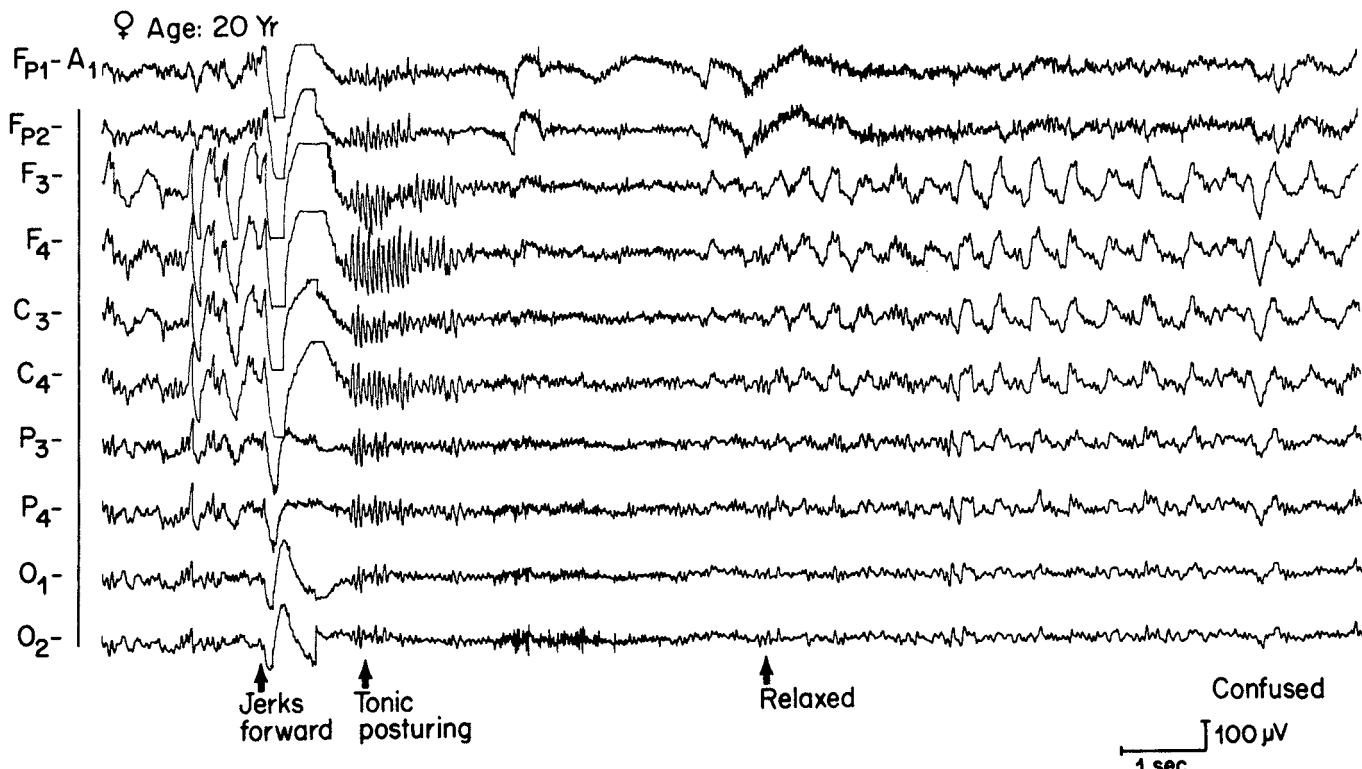
### Tonic-Clonic

A generalized tonic-clonic seizure is more frequently of partial onset, with the GTC as the final common pathway of seizure propagation. Nonetheless, primary GTCs may also occur as part of the seizure repertoire in primary idiopathic generalized epilepsy syndromes including CAE and JME. The seizure has two distinct phases, first a tonic phase with generalized

agonist-antagonist muscle coactivation, followed by a progressively slowing generalized clonic phase of muscle movements involving repetitive clonic contraction directly followed by gradually longer relaxation phases, until a state of deep postictal sleep and unresponsiveness ensues, frequently with loss of bladder and/or bowel continence. Tongue laceration from biting is frequent. While most GTCs last 90 seconds or less in duration, persistence beyond 5 minutes should be considered a medical emergency with treatment initiation for status epilepticus. Ictal EEG shows initial generalized polyspikes building up to a frequency of approximately 10 Hz (the so-called epileptic recruiting rhythm) during the tonic seizure phase, followed by a generalized spike-wave pattern that gradually slows to a frequency of 1 Hz coinciding with the clonic seizure phase, and ultimately postictal suppression following seizure termination (Fig. 8-8A–D; see also *Practical Guide: EEG*, Fig. 10-19).

### PARTIAL-ONSET SEIZURES

Partial-onset seizures are sub-classified further as simple or complex partial, depending upon whether or not consciousness is affected. The ictal EEG demonstrates characteristic spatiotemporal evolution of initially focal rhythms that progressively



**Figure 8-7.** Tonic seizure associated with poly-spikes (beta activity). (From Wyllie E et al. *The Treatment of Epilepsy: Principles and Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2006:178; Figure 12.10, with permission.)

increase in amplitude while slowing in frequency, and spread to neighboring electrode derivations and beyond (Fig. 8-9A–C; see also *Practical Guide: EEG*, Figs. 10-8 and 10-9). Seizures may be considered as subclinical if they have no subjective or objective clinical accompaniment, or clinical in expression if they do have an overt accompaniment. Subclinical seizures are of interest predominantly in epilepsy syndrome classification and may also have prognostic importance when surgery is being considered, since subclinical seizures that colocalize to the surgical epileptic focus have better prognosis for outcome than those that are not colocalized.<sup>32</sup> However, clinical seizures that can be verified as representing that patient's habitual clinical seizure type out of the hospital have most importance in determining epilepsy syndrome diagnosis, as well as for presurgical planning.<sup>33</sup>

### Simple Partial Seizures

In a simple partial seizure, consciousness is preserved. Clinical expression of simple partial seizures is heterogeneous and depends upon lobe/region of cerebral onset. The term aura is still also used frequently, especially by patients, to describe a simple partial seizure beginning in the occipital, temporal, or parietal cortex, since the symptoms involved are subjective visual, cognitive/emotional, or sensory, and may serve as a warning to the patient prior to progression of the seizure into lost or altered consciousness as the seizure discharge propagates beyond the region of initial onset. Simple partial seizures of frontal lobe origin most often have an objective expression of focal posturing and clonic motor movements. While focal atonia with weakness are common postictal signs (Todd's paralysis), they may also rarely be seen during an electroencephalographic ictus.<sup>22</sup>

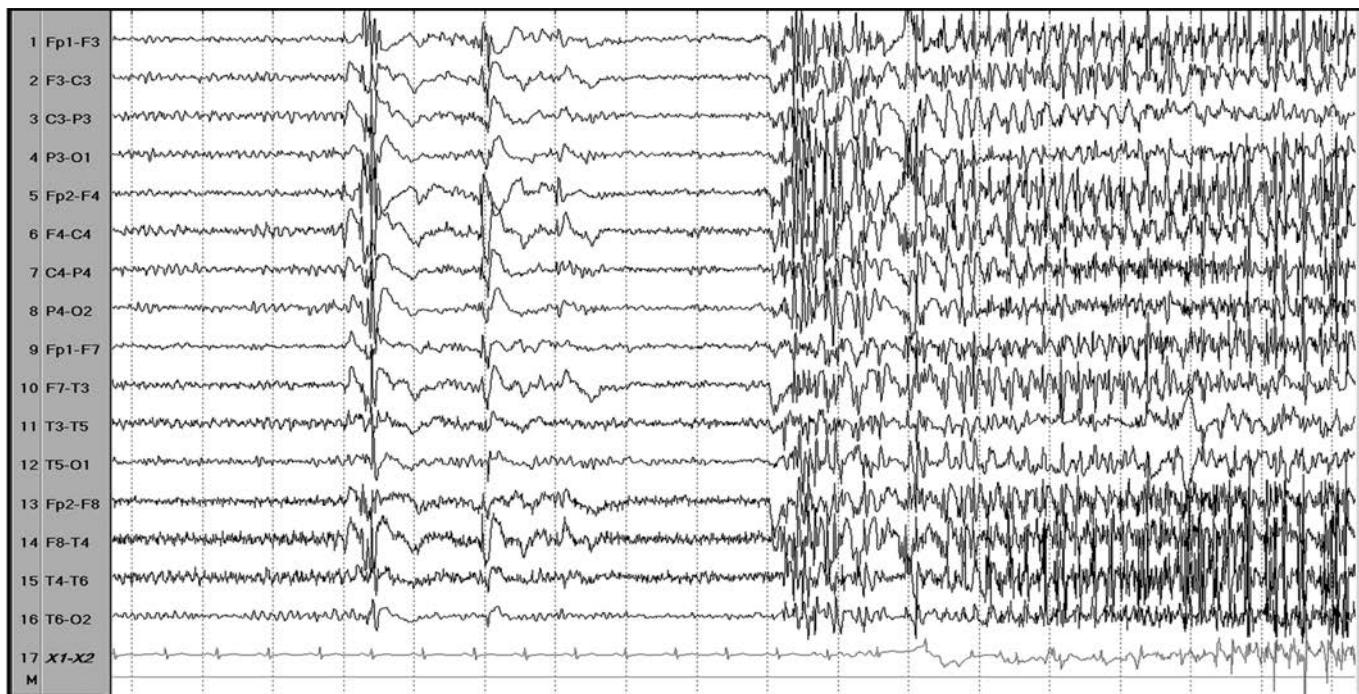
EEG during a simple partial seizure may often be normal, or demonstrate focal evolving rhythmic discharges without spread to other areas.

### Complex Partial Seizures

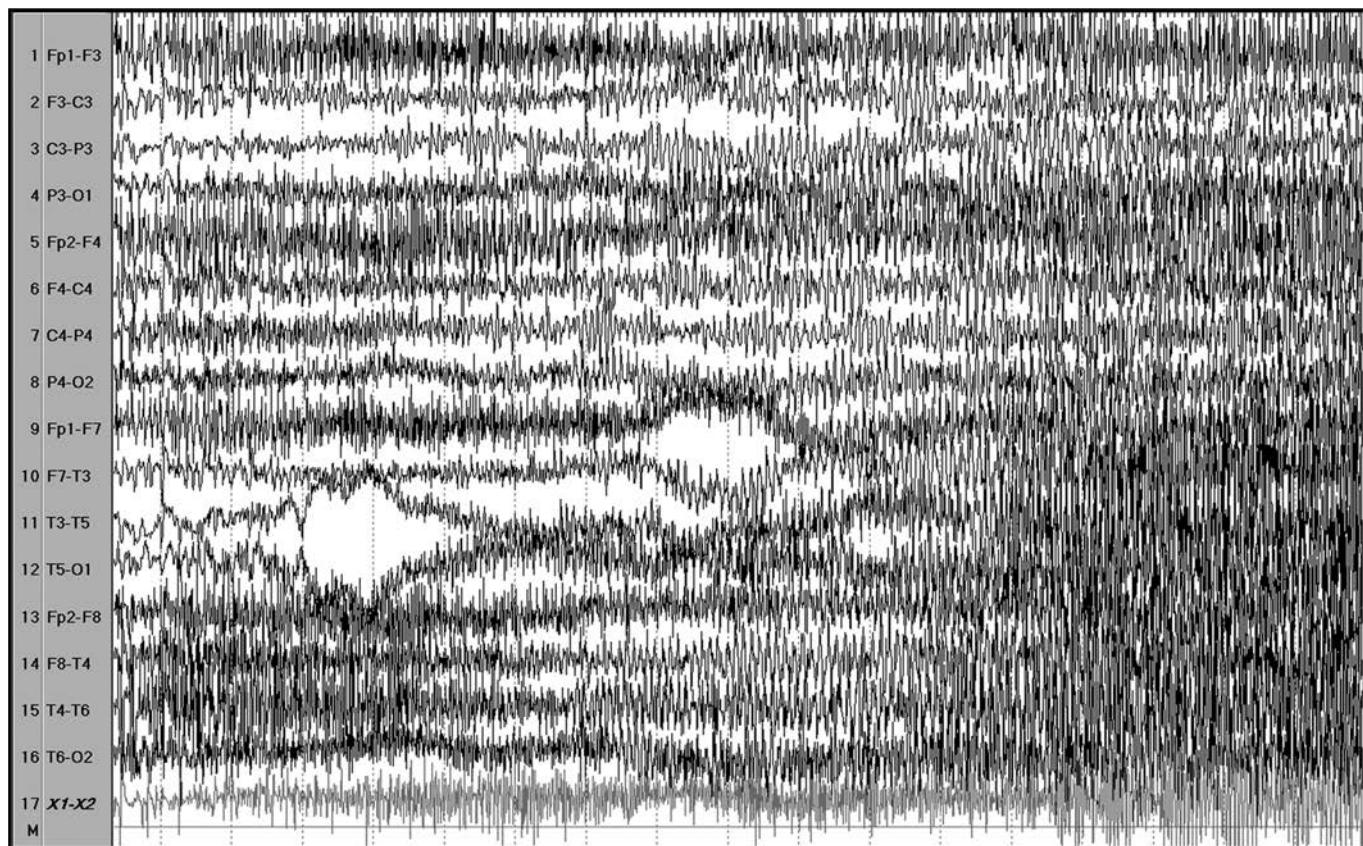
A complex partial seizure by definition features consciousness loss or alteration. Clinical behavior depends upon lobe of onset.

**TEMPORAL LOBE SEIZURES.** Temporal lobe onset seizures most frequently show staring, behavioral arrest, and automatisms of the mouth, face, and limbs such as lip smacking, repetitive swallowing, tongue thrusting, vocalization, or aimless fumbling hand/finger movements. Aimless walking and falls are possible. As the seizure propagates, head turning and limb posturing are frequent. Head turning is most often toward the seizure focus initially (ipsiversive), followed by head and/or body/trunk deviation away from the seizure focus late in the course (versive turning).<sup>29,33</sup> Limb posturing may be asymmetric, involving a still and dystonic hand posture contralateral to the seizure focus and a hand/arm with mobile automatisms ipsilateral to the focus. The ictal EEG pattern usually consists of rhythmic theta/delta, beta, or alpha activity from temporal region with progressive change of frequency involving wider areas as the seizure evolves (see *Practical Guide: EEG*, Fig. 10-9).

**EXTRATEMPORAL SEIZURES.** Seizures of extratemporal origin (frontal, parietal, or occipital lobes) may have features similar to temporal lobe seizures. However, extratemporal seizures more often will have prominent axial and proximal limb movements that lead to mobilization of the patient and falls

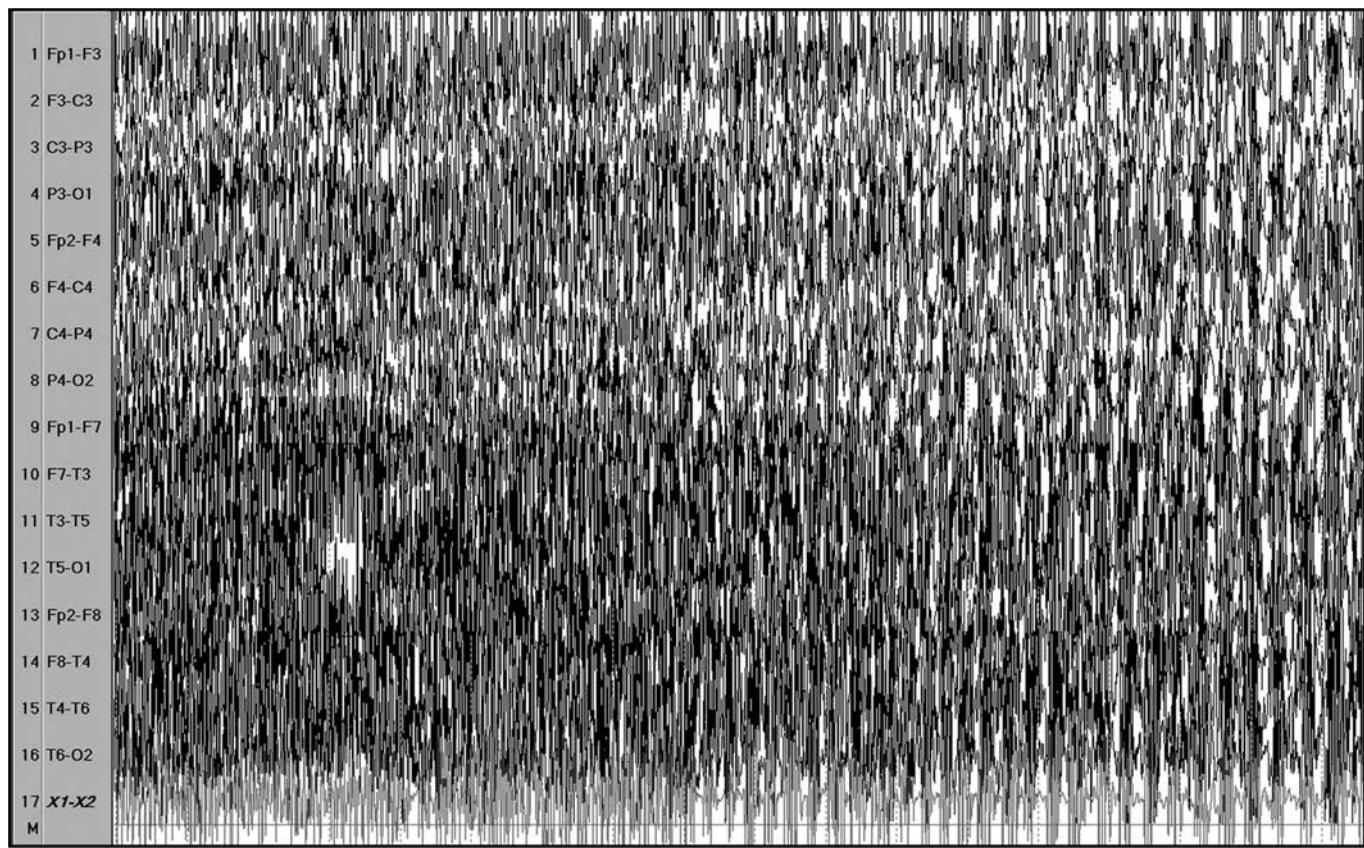
**A**

**Figure 8-8.** Tonic-clonic seizure. The EEG waking background is normal immediately prior to ictal onset. Seizure onset is shown in second 10 of the first epoch. The first change is generalized polyspike and spike-wave activity, followed by iterative polyspike discharges at a frequency of approximately 10 Hz (see epoch 1, Fig. 8-8A above, the epileptic recruiting rhythm) evolving further into generalized spike-wave activity that is mostly obscured by muscle and movement artifact (epoch 2, Fig. 8-8B, page 157) that progressively slows in frequency (epochs 3–4, Figs. 8-8C–D, pages 158–159), ultimately culminating in seizure cessation with following postictal generalized background attenuation and suppression (epoch 5, Fig. 8-8E, page 160). The clinical accompaniment was sudden adduction, flexion, and stiffening of both upper extremities during the tonic seizure phase, followed by symmetrical upper limb extension and eventual rhythmic clonic movements of all four limbs that progressively slowed in frequency until termination, followed by postictal sleep and sonorous respirations. (Sensitivity: 10  $\mu$ V/mm, HFF: 35 Hz, LFF: 1.6 Hz, 18-second epoch).



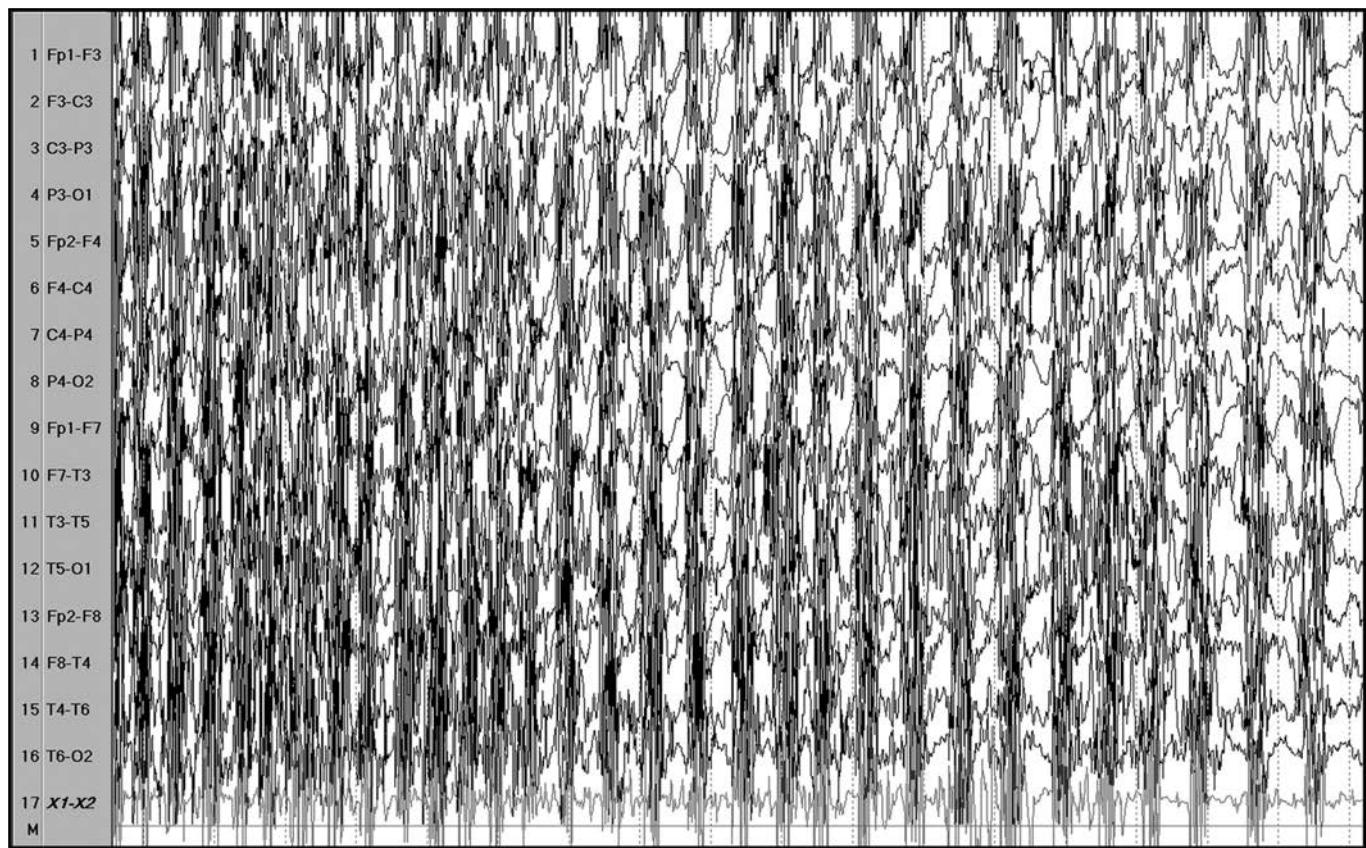
B

**Figure 8-8. Cont'd.**

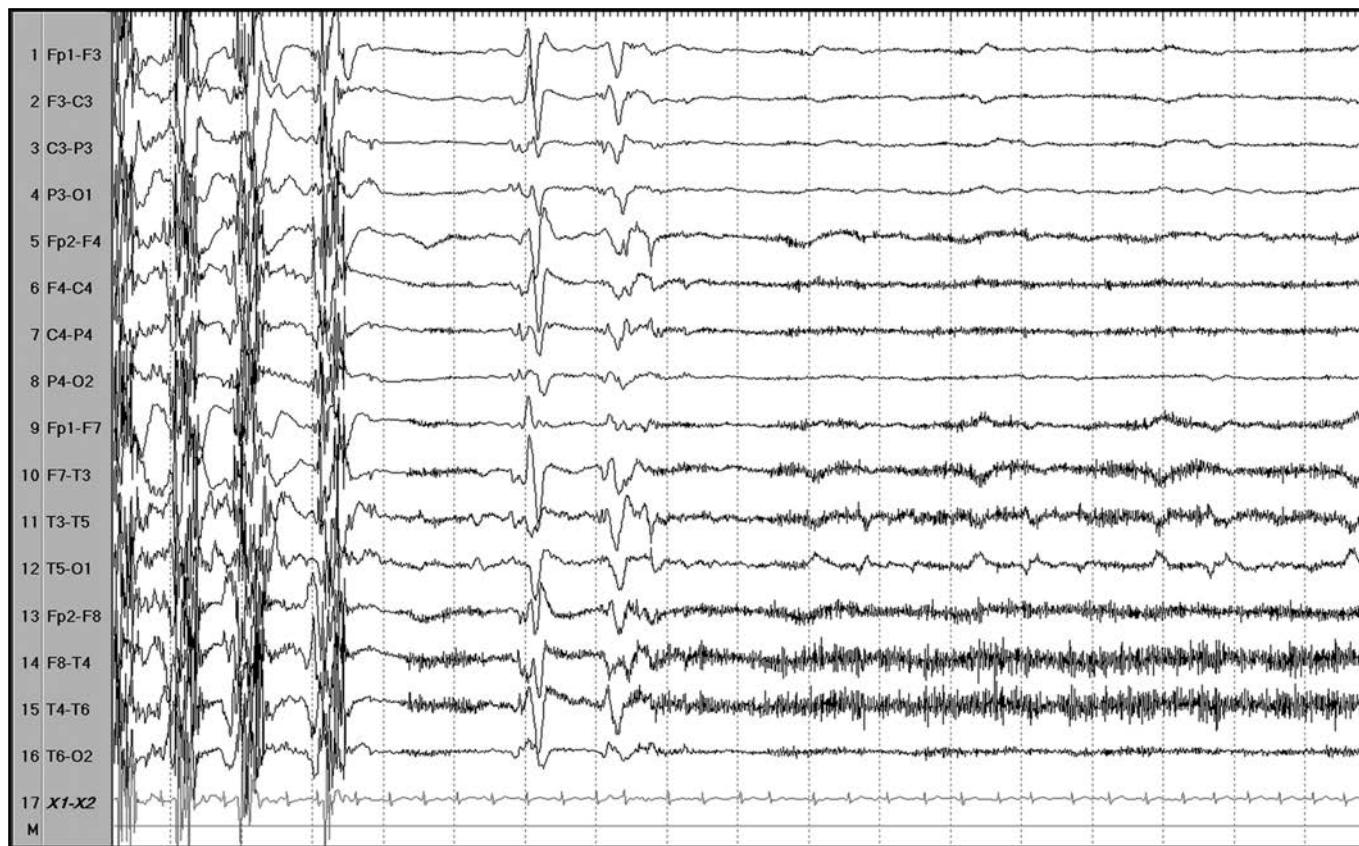


**C**

**Figure 8-8. Cont'd.**

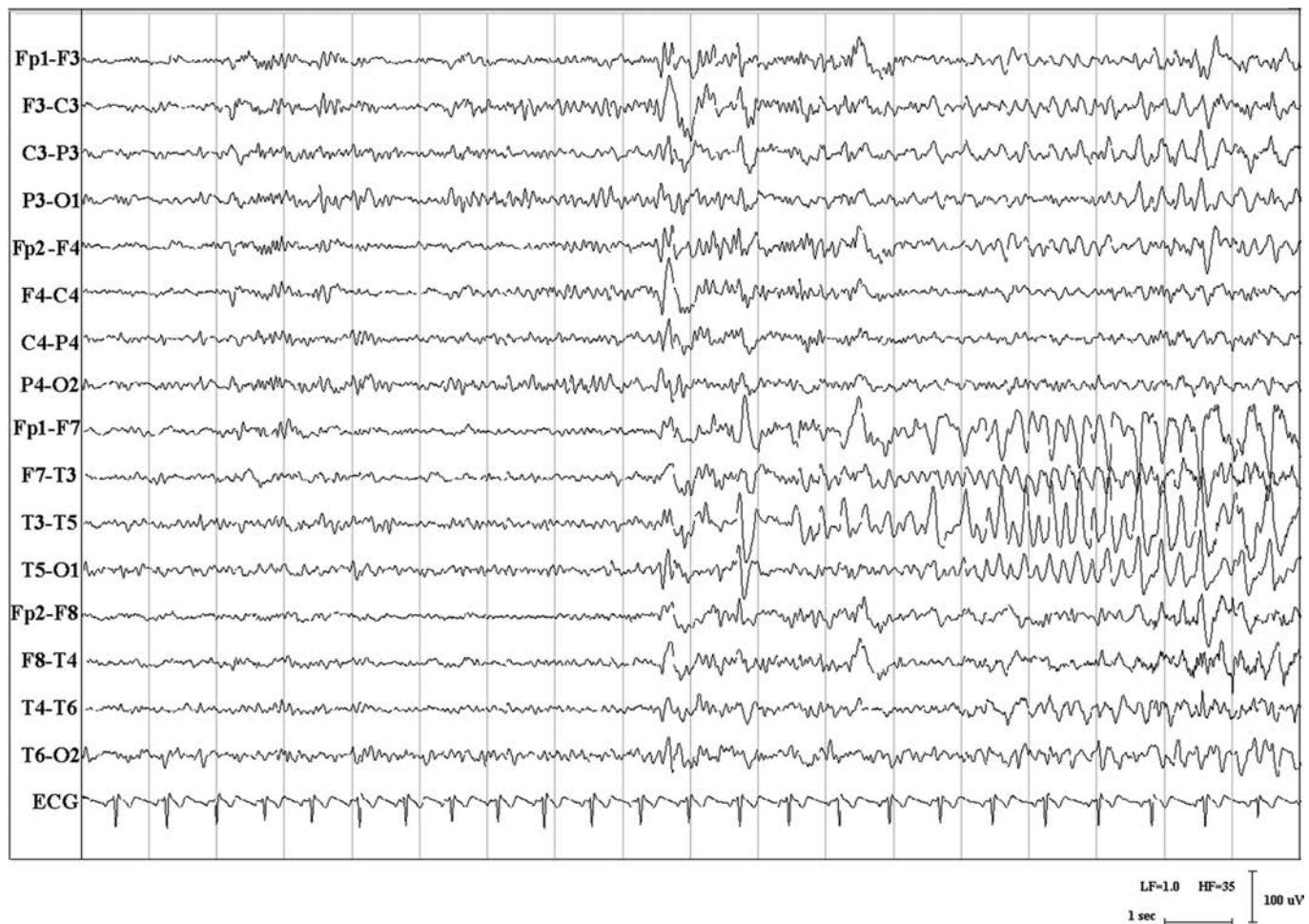


**Figure 8-8.** Cont'd.

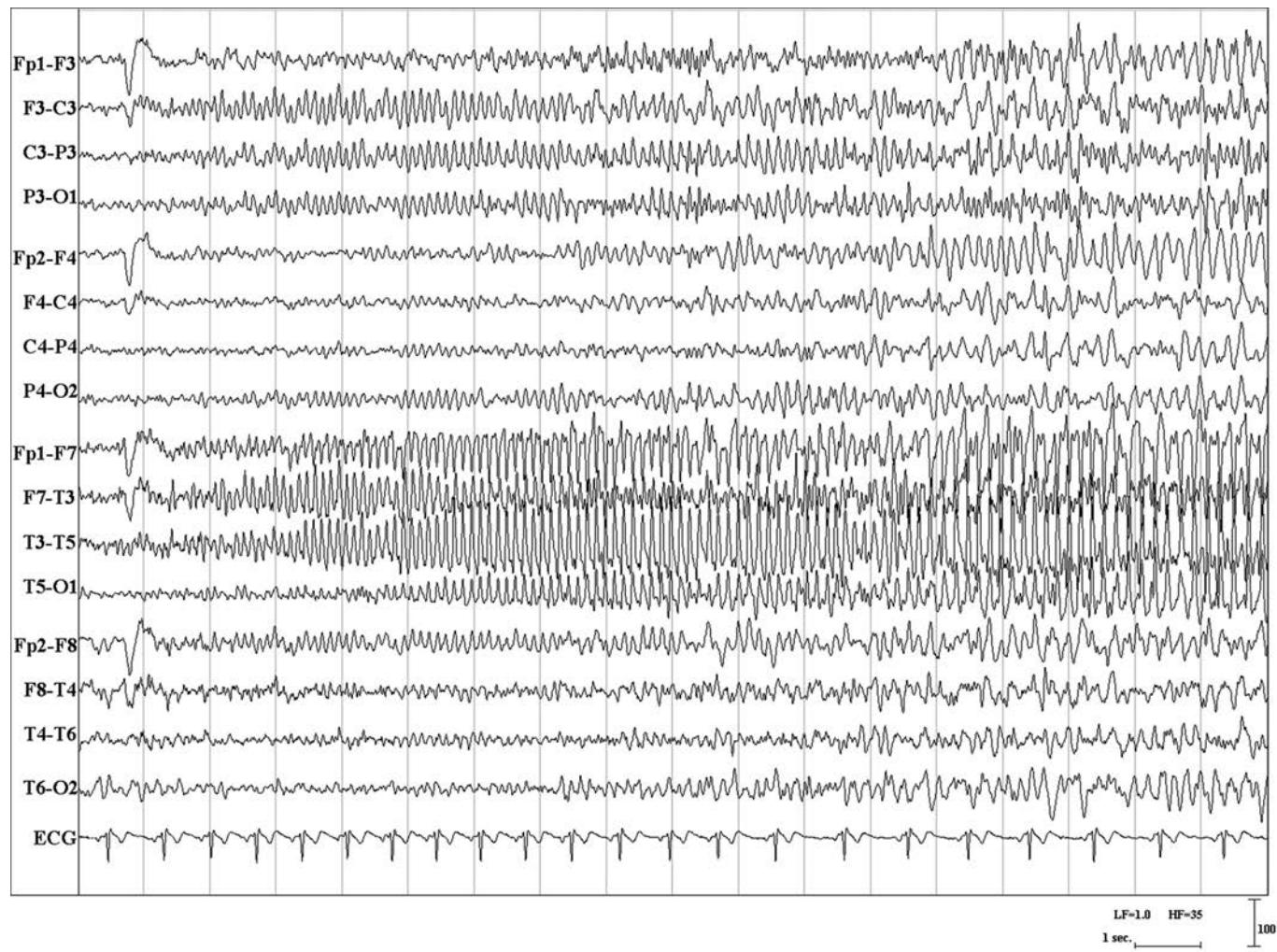


E

**Figure 8-8. Cont'd.**

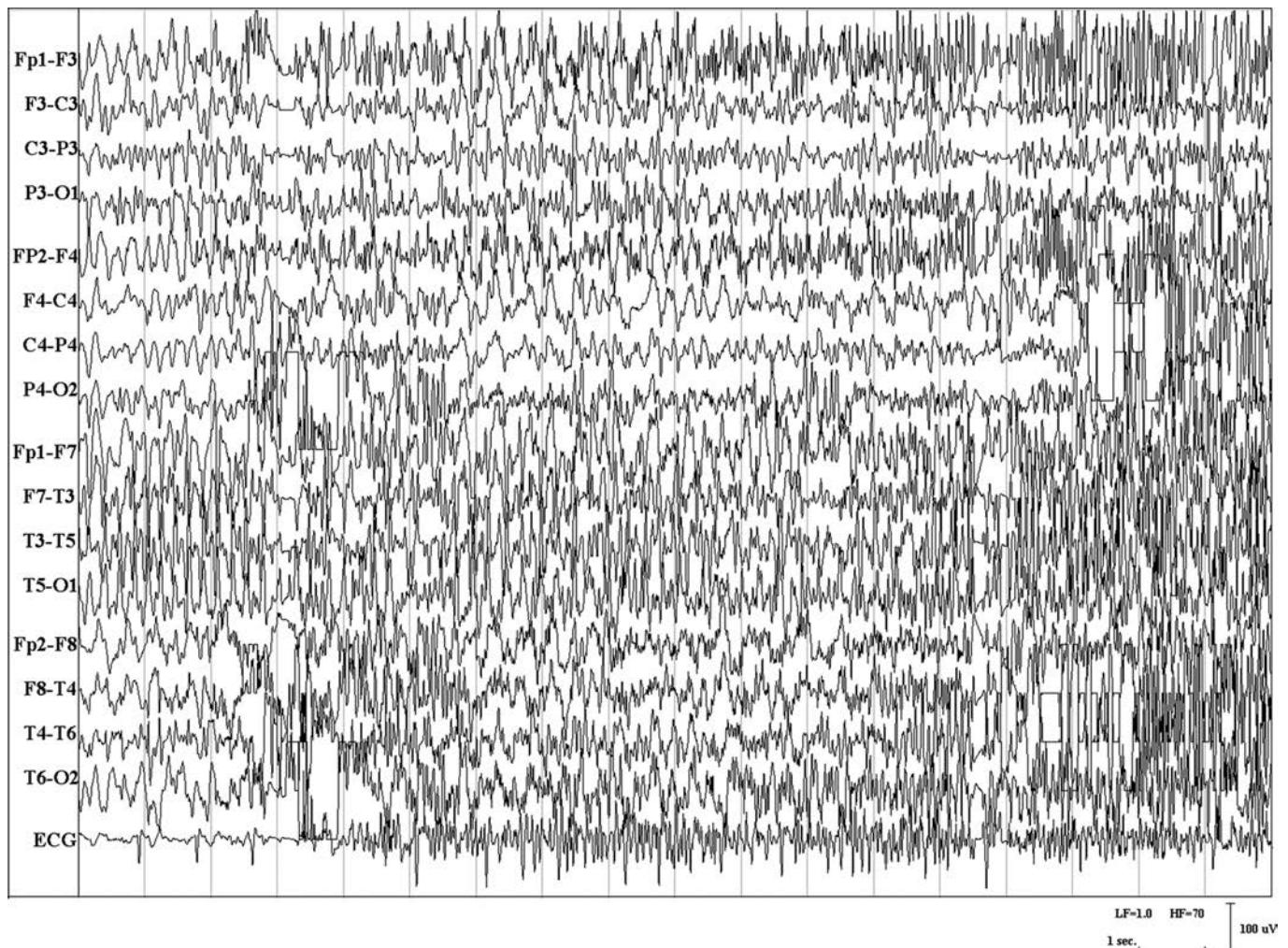
**A**

**Figure 8-9.** A partial seizure of left temporal lobe onset. The EEG background shows normal N2 sleep prior to ictal onset in second 10 of the first epoch (see epoch 1, Fig. 8-9A above). The first change is focal rhythmic activity localized to the left anterior and midtemporal region, followed by spatiotemporal evolution of the discharge as it progressively increases in amplitude and grows slower in frequency, spreading to neighboring left frontotemporal and parasagittal electrode derivations (epoch 2, Fig. 8-9B, page 162), and eventually beyond to the entire head surface (epoch 3, Fig. 8-9C, page 163). The clinical accompaniment was staring with behavioral arrest, oroflagrammatic automatisms characterized by aimless lip smacking and chewing movements, then dystonic posturing of the right hand and flowing manual automatisms of the left hand. Subsequent left anterior temporal lobectomy surgery rendered the patient seizure-free. (Sensitivity: 5  $\mu$ V/mm, HFF: 70 Hz, LFF: 1.0 Hz, 18-second epochs).



**B**

**Figure 8-9. Cont'd.**



C

**Figure 8-9. Cont'd.**

from bed, bizarre and sometimes violent limb flailing movements that may be misdiagnosed as psychogenic (the so-called hyperkinetic or hypermotor seizures), and more frequently arising from the sleep state.<sup>29,33,34</sup> Ictal EEG during extratemporal seizures may show localization to a lobe or region but more commonly shows only minimal rhythmic background change or is obscured by muscle and movement artifact (Fig. 8-10A–F; see also *Practical Guide: EEG*, Fig. 10-7).

### SECONDARY GENERALIZED TONIC-CLONIC

Partial seizures that propagate to both cerebral hemispheres may become secondary generalized convulsions. Immediately prior to secondary generalization, the contralateral arm may become fully extended, while the ipsilateral arm is flexed at the elbow, making the so-called figure-4 sign.<sup>29,33,35,36</sup> The most reliable point of assessing the lateralizing significance of head turning and body posturing movements relative to the side of seizure onset (i.e., lateralization) is immediately prior to the onset of the clonic seizure phase.<sup>29,35,36</sup> Clinical phenomena are otherwise similar to that described for primary GTCs, and the two types can be quite difficult to differentiate even during detailed video-EEG monitoring, so the distinction may instead

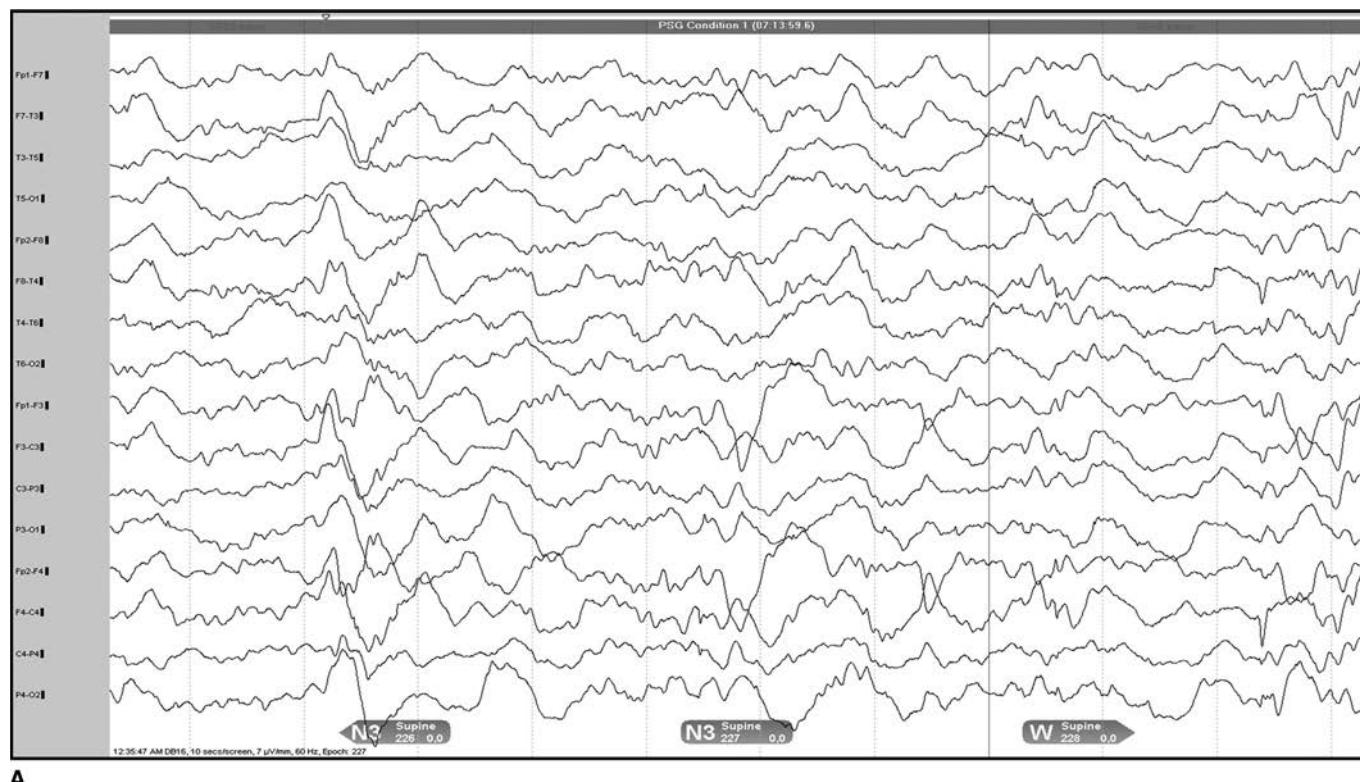
necessarily depend upon other variables such as structural or functional imaging tests, interictal EEG abnormalities (see *Practical Guide: EEG*, Fig. 10-10), and neuropsychological data.

### SEIZURES IN INFANT AND PEDIATRIC VIDEO-EEG MONITORING

Infants display a range of other potential ictal semiologies with partial or generalized onset seizures. A detailed review of the full range of neonatal, infantile, and pediatric seizure types and their accompanying EEG patterns is beyond the scope of this chapter, and the interested reader is referred to other recent sources describing epilepsies and seizure types with both benign, presumably genetic mechanisms, as well as refractory and enduring courses.<sup>37–42</sup> However, infantile spasms are of sufficiently common occurrence and a clinically vital entity to be distinguished from other neonatal spells and seizure types, so as to merit inclusion herein.

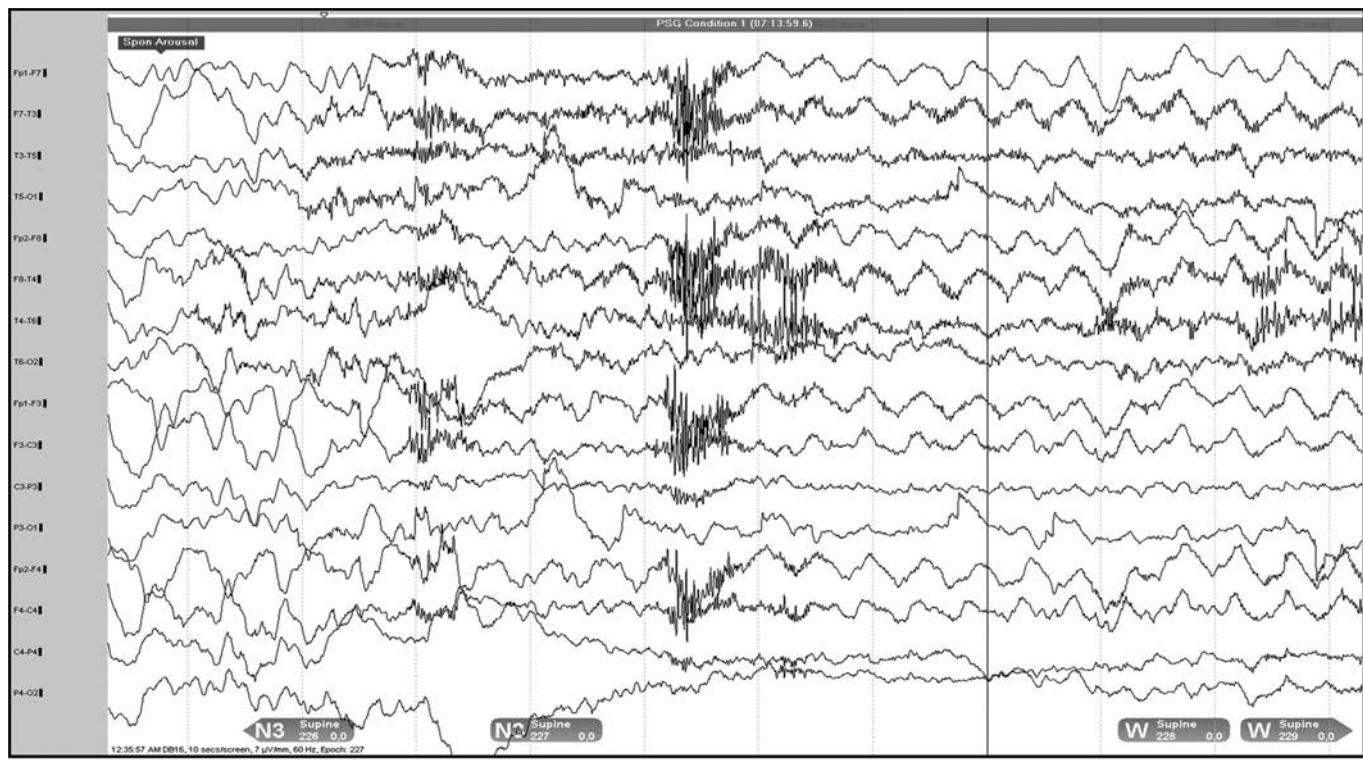
#### *Infantile Spasms and the West Syndrome*

Infantile spasms, generalized atonic/astatic seizures involving loss of postural tone and sudden head nodding or collapse,



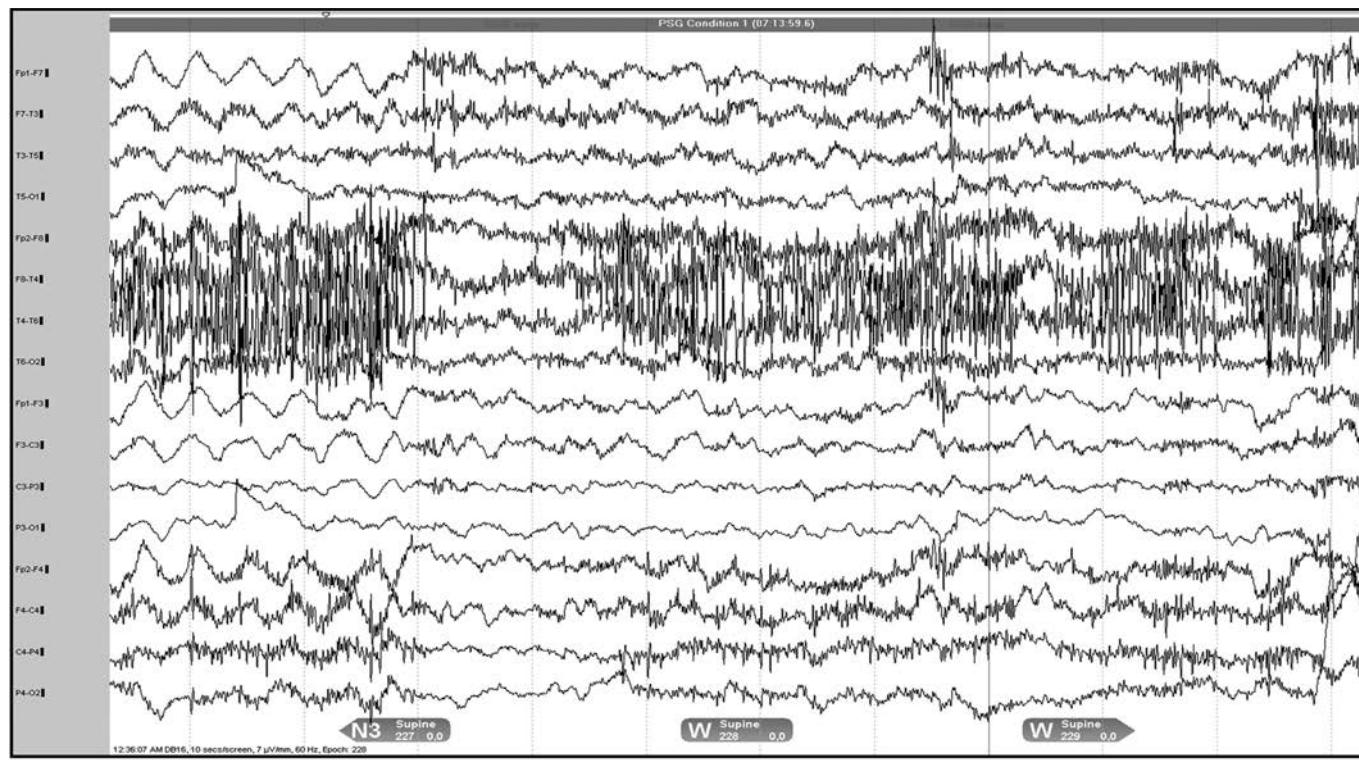
A

**Figure 8-10.** A partial seizure of extratemporal frontal lobe onset. EEG demonstrates normal N3 sleep just prior to ictal onset (see epoch 1, Fig. 8-10A above). Seizure onset is shown in second 1 of epoch 2 (see Fig. 8-10B, page 165) with the first evident change being spontaneous arousal with subtle diffuse rhythmic theta activity, evolving to nonlateralized bifrontally dominant rhythmic delta frequency activity (sixth to eighth second of epoch 2) that gradually becomes less organized (epochs 3–5, Figs. 8-10C–E, pages 166–168) and eventually terminates with resumption of generalized theta background slowing during drowsy wakefulness in the postictal state (epoch 6, Fig. 8-10F, page 169). The clinical accompaniment was explosive onset of bilateral proximal upper limb abduction with screaming vocalization, lasting approximately 15 seconds, and abrupt termination without obvious postictal somnolence. (Sensitivity: 7 µV/mm, HFF: 70 Hz, LFF: 0.5 Hz, 12-second epoch shown).



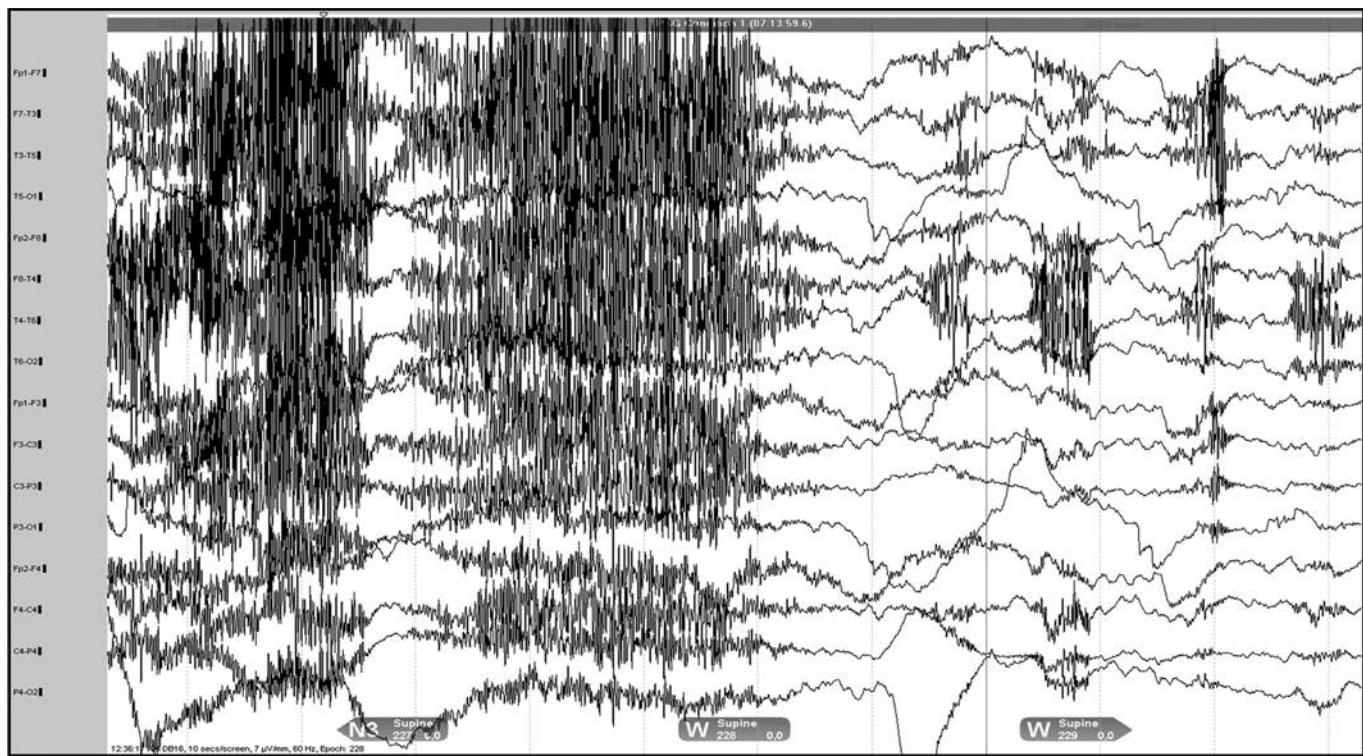
B

Figure 8-10. Cont'd.



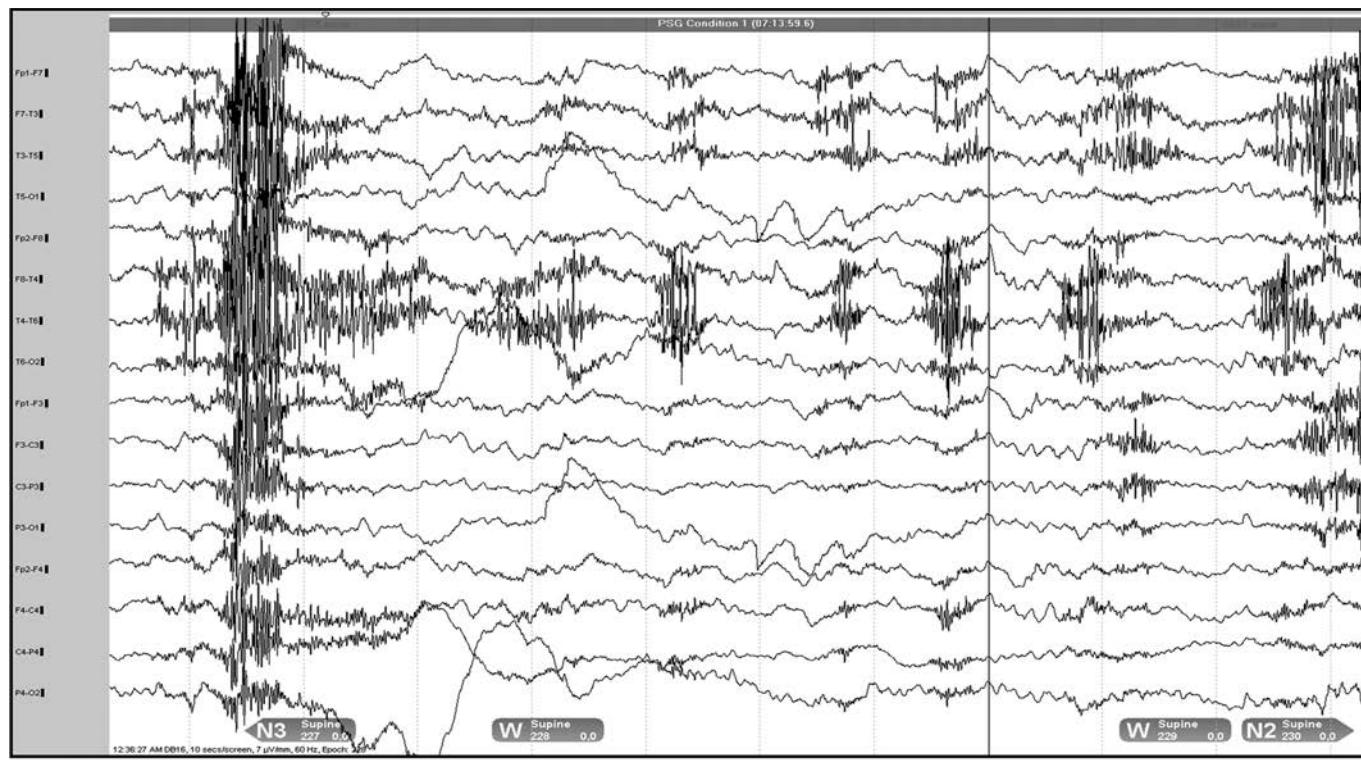
C

**Figure 8-10. Cont'd.**



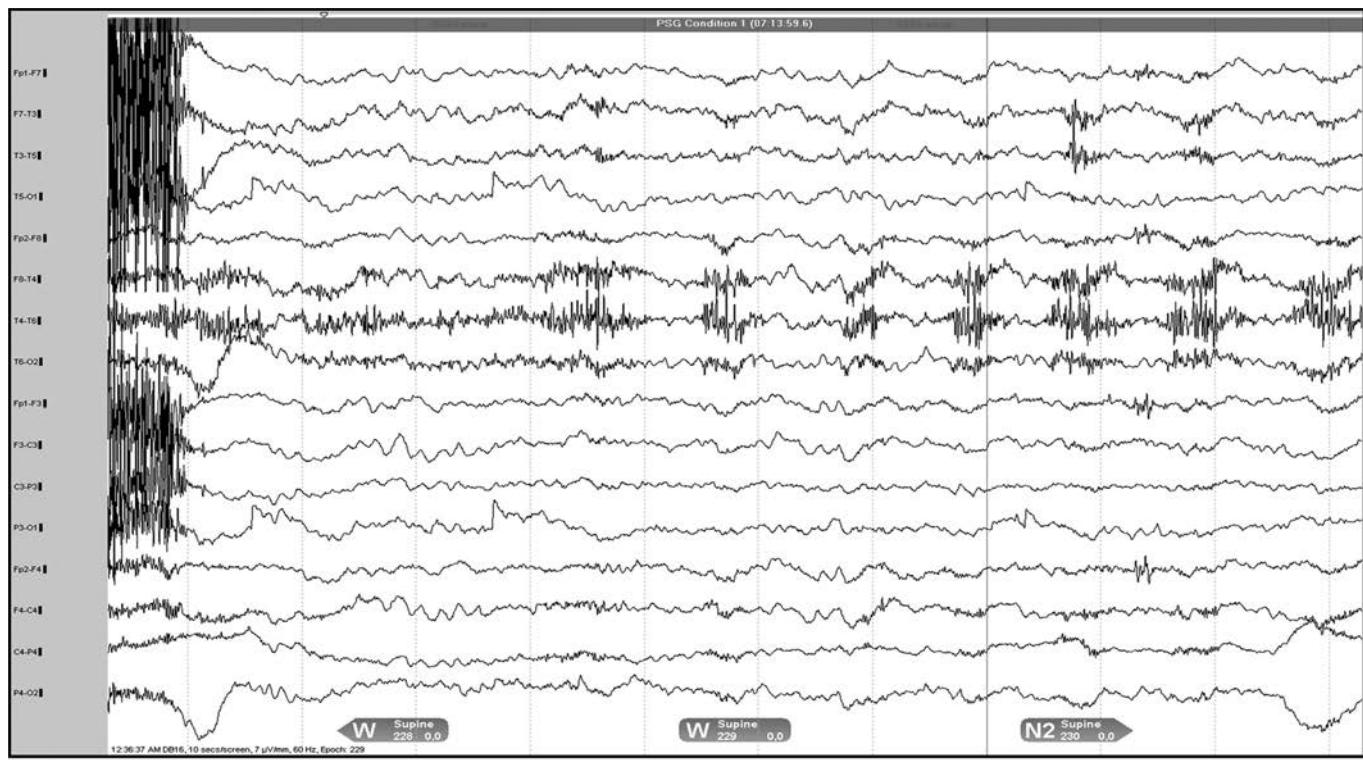
D

Figure 8-10. Cont'd.



E

Figure 8-10. Cont'd.



F

Figure 8-10. Cont'd.

		Common Clinical Characteristics Differentiating Partial and Generalized Epilepsy Syndromes			
		Partial		Generalized	
		<i>Idiopathic</i>	<i>Cryptogenic/Symptomatic</i>	<i>Idiopathic</i>	<i>Cryptogenic/Symptomatic</i>
<b>Age of onset</b>	Childhood		Any	Childhood/Adolescence	
<b>Seizure types</b>	Any partial		Any partial	Absence Myoclonic GTC	
<b>Natural history</b>	Remits by teens		Variable	Remits (CAE) or lifelong (JAE,JME)	
<b>Typical response to drug therapy</b>	Excellent		Variable	Good	
<b>Etiology</b>	Genetic		Unknown/Variable	Genetic	
<b>Imaging findings</b>	Normal		Variable	Normal	
<b>Family history of epilepsy</b>	Yes		Variable	Yes	
					Usually none

often with forward arm extension (leading to the previous term of “Salaam attacks”) occur as part of the West syndrome (infantile spasms, developmental delay, and hypsarrhythmic EEG background). Ictal EEG shows an electrodecremental pattern with generalized background attenuation. Interictal EEG typically shows hypsarrhythmia with frequent generalized and multifocal IEDs superimposed upon a high-voltage, chaotic, and disorganized background (likened to “scrambled eggs” by many EEGers) (see *Practical Guide: EEG*, Figs. 10-26 to 10-28). Prognosis is poor for return to a normal development, but prompt treatment with ACTH, other steroids, or vigabatrin in a subset of patients may affect an excellent outcome with dramatic improvement of EEG. Future evolution into a symptomatic generalized epilepsy syndrome such as Lennox-Gastaut syndrome is frequent.

### SYNTHESIZING THE EPILEPSY SYNDROME: INTEGRATING VIDEO-EEG DATA INTO THE CLINICAL PICTURE AND OTHER APPROPRIATE INVESTIGATIONS

The gold standard for seizure classification is seizure capture and analysis by video-EEG monitoring. Nonetheless, other clinical and ancillary data are considered in the overall epilepsy syndrome diagnosis for an individual patient, particularly when the video-EEG data themselves are unclear concerning whether the seizures are primary generalized or partial in onset. Clinical characteristics such as the patient’s age of seizure onset, the range of different seizure types involved (both as determined historically and objectively from video EEG monitoring), the natural history of seizures and their response to AED therapies, the presence of a known etiology, a family history of epilepsy, and the neurological examination are all important factors to consider (Table 8-2). Increasingly, application of structural or functional imaging tests often helps clarify the lobe of onset in partial epilepsy syndromes, and to help differentiate primary generalized from extratemporal frontal lobe epilepsies with rapid secondary bilateral synchrony.<sup>25,26,43</sup>

### PITFALLS IN VIDEO-EEG MONITORING

Video-EEG monitoring is a highly reliable means of differentiating spells and seizures and appropriately diagnosing a patient’s epilepsy syndrome. However, like any clinical test, video-EEG is subject to limitations. First, the technique is dependent upon capturing the patient’s habitual clinical spell. If this spell does not occur during the monitoring session, “all bets are off” with regard to diagnosis. Second, the test has limited specificity just as interictal EEG. Qualitative interictal abnormalities and conclusions regarding monitored spells are subject to considerable variation in interpretation even among experienced clinicians. Considerable training and experience is necessary to accurately employ the technique. Third, technical frustrations are frequently encountered, including electrode disconnection or artifact, and the patient must be kept on camera as much as is feasible, since important clinical data can be lost when spells/seizures occur off camera such as during bathroom breaks. If possible, providing a day room with video capabilities where patients can still be observed but in a different environment can be helpful. Though somewhat objectionable, mounting cameras in bathrooms also can limit such losses. Last, it must be realized that just like laboratory EEG, the diagnosis of epilepsy cannot be made or excluded solely on the basis of interictal data. That is, one cannot accurately conclude that a diagnosis of epilepsy is excluded by several days of normal interictal EEG data, even under optimal recording and interpreting circumstances, since a substantial minority of patients with true epilepsy lack IEDs between seizure events.

### CONCLUSIONS

Video-EEG monitoring is a valuable diagnostic tool in clinical epilepsy practice. It readily allows distinction of a variety of paroxysmal spells, including common nonepileptic mimickers of epilepsy such as PNESs and syncope. For refractory epilepsy patients, it also enables appropriate classification of primary

generalized or partial-onset seizure types, yielding crucial information for patients and their treating physicians concerning prognosis and informing treatment options. When seizures are difficult to quantify, video-EEG also allows an objective measure of seizure frequency that can help tailor treatment intensity. The main limitations of video-EEG include its dependency on spell capture and limitations in the yield of even prolonged interictal recording. In conclusion, video-EEG remains the gold standard for seizure classification and localization in epilepsy care. When considered in the context of the patient's unique clinical history and accompanying interictal EEG and imaging data, video-EEG monitoring may yield crucial information informing patient prognosis, counseling, and treatment.

## ACKNOWLEDGMENTS

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# Invasive Video EEG Monitoring in Epilepsy Surgery Candidates: Indications, Technique, and Interpretation

## INTRODUCTION

Epilepsy is a common neurologic condition that affects people of all ages, is costly to the individual and society, and is frequently resistant to medication. The diagnosis of epilepsy depends upon a thorough medical history and performance of a neurologic examination, supplemented with electroencephalographic (EEG), imaging studies and other data. Prolonged inpatient scalp video EEG (sVEEG) monitoring is often used to confirm the diagnosis of epilepsy and localize seizure onset in potential candidates for surgical treatment. However, noninvasive testing occasionally fails to adequately localize the patient's seizures, requiring consideration of invasive video EEG (iVEEG) monitoring. This chapter will review the indications, recording techniques and interpretation of iVEEG.

## DEFINITIONS

Epilepsy is the tendency to have recurrent, unprovoked seizures that result from either a genetically based condition or an acquired injury to the brain. Acquired causes (including pre- or perinatal injury, infection, trauma, tumor, and stroke) vary in prevalence by age. Often, a specific underlying etiology is not found despite thorough investigation. Epilepsy is distinguished from acute symptomatic seizures, which are seizures produced in an otherwise normal brain in response to an acute provoking stress such as medication reaction, systemic illness, or metabolic disturbance.<sup>1,2</sup>

A seizure is a paroxysmal event marked by excessive neuronal activity in a population or network of neurons, with associated clinical or behavioral change. The behavioral change may range from a simple feeling or a perception (as with simple partial seizures), to unawareness with automatic movements (complex partial seizures), to whole-body convulsive activity

(generalized tonic-clonic seizures). Seizures are subclassified according to their electrophysiologic and clinical properties into generalized (whole brain) and partial (localized) onset.<sup>3</sup> Due to their localized nature, partial-onset seizures are most amenable to surgical therapy. Their clinical features, and thus their anatomic localization, provide important initial clues that will ultimately guide the performance of iVEEG and surgical decision-making.

Drug-resistant epilepsy can be considered when a patient has failed to achieve seizure freedom after two trials of medication used alone or in combination, appropriately chosen for the seizure type, taken appropriately, and tolerated by the patient.<sup>4</sup> For example, a study has shown that 47% of patients with newly diagnosed epilepsy achieved seizure freedom on the first medication,<sup>5</sup> and an additional 20% became seizure free with the second or the third medication. Of those who failed to become seizure free on trials of two or more medications, only 4% eventually became seizure free with further medications, leaving over 36% of epilepsy patients drug resistant. Another study suggests caution when considering drug-resistant epilepsy, pointing out that as many as 15% of patients with drug-resistant epilepsy will experience at least a 6-month seizure free period over 3 years of follow-up,<sup>6</sup> though seizures often recur upon longer follow-up. Thus, the majority of patients who continue to have seizures despite trials of two or more medications will continue to have seizures and should therefore be advised of, and evaluated for, possible surgical treatment.

Drug-resistant epilepsy is costly to the patient, the health-care system, and society in general.<sup>7,8</sup> Cost for drug-resistant epilepsy accrues from both direct medical expenses (diagnostic tests, treatment, office visits, emergency room visits, hospitalizations), and from indirect sources (un- or underemployment, lost educational opportunities, missed days of work, premature mortality).<sup>9</sup> Patients with drug-resistant epilepsy are also legally restricted against operating motor vehicles, and many patients

experience impaired quality of life in the home, school, and workplace.<sup>10</sup> Epilepsy surgery, especially when successful at controlling seizures, can be a cost-effective treatment option with significant impact on the quality of life.<sup>11-14</sup>

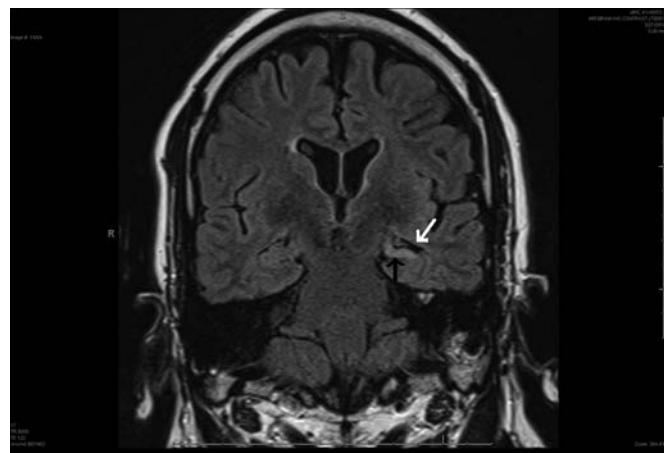
Epilepsy surgery can be broadly defined as an operative procedure whose primary goal is to alleviate, ideally eliminate, seizures. This distinguishes it from lesion surgery (e.g., tumor resection) where the primary goal of the operation is to remove or ameliorate a lesion, with seizure control perhaps a secondary goal. The principal determinant of good outcome from epilepsy surgery is the careful selection of patients likely to do well. In many patients, iVEEG plays a vital role in this selection.

## INDICATIONS FOR INVASIVE VIDEO EEG

Evaluation for epilepsy surgery is indicated if the patient has drug-resistant seizures, localized in onset (larger-scale disconnection operations such as corpus callosotomy, hemispherectomy and hemisphericectomy are beyond the scope of this chapter; the interested reader is directed to recent reviews<sup>15-17</sup>), ideally arising from a single area, which can be safely and effectively resected by the neurosurgeon. The single most common form of epilepsy surgery is the anterior temporal lobectomy, since mesial temporal lobe epilepsy (with seizures originating from the hippocampus and other structures deep in the middle of the temporal lobe) is common, and is often drug resistant.<sup>18</sup> The mesial temporal lobe proves to be a relatively safe area on which to operate, with a high chance of seizure freedom. Seizures from this area are usually accompanied by loss of normal memory function, however, and unilateral temporal lobectomy does not further threaten this important ability. Seizures arising outside the mesial temporal lobe (including those from the temporal lobe surface—or neocortex—and other lobes of the brain) pose greater challenges and may yield lower postoperative outcomes.

## THE NONINVASIVE EVALUATION

All patients undergoing iVEEG will have undergone a thorough noninvasive evaluation that focuses on localizing seizures and determining areas of brain function and dysfunction. This typically begins with an evaluation by an epileptologist (a neurologist specially trained in epilepsy), where relevant history is gathered and a neurologic examination performed. The two most helpful diagnostic studies are ictal sVEEG (see Chapter 8; also see *Practical Guide: EEG*, Chapter 10) and magnetic resonance imaging (MRI). The MRI procedure should be tailored to the patient's individual needs. For example, when investigating seizures that may arise in the temporal neocortex or mesial temporal lobe a seizure protocol MRI is warranted, in which thin image slices are made perpendicular to the long axis of the temporal lobe (i.e., tilted in orientation from the standard coronal plane). When seizures are suspected to arise outside the temporal lobe, attention can be focused on the appropriate area based on the seizure semiology. For example, suspicion that seizures arise from the frontal lobe should draw the neuroradiologist's attention to this area. Higher-fidelity MRI scans (3.0 T and above) tend to improve the signal-to-noise ratio and may provide additional information compared to 1.5-T MRI.<sup>19,20</sup> Findings may include hippocampal sclerosis



**Figure 9-1.** MRI of the brain showing left mesial temporal sclerosis, marked by volume loss and high signal of the hippocampus (*dark arrow*), and compensatory enlargement of the temporal horn of the lateral ventricle (*white arrow*). Performed with a 1.5-T MRI, FLAIR sequence, with 3.0-mm slices perpendicular to the axis of the temporal lobe.

(Fig. 9-1), vascular malformations, tumors, traumatic lesions, and malformations of cortical development, though the MRI is often normal.

Other noninvasive studies often found complementary to sVEEG and MRI include neuropsychological testing, functional imaging, and magnetoencephalography (MEG). Neuropsychological testing involves the administration of a large set of specific cognitive tests of memory, attention, language, and other functions. Deficits can serve to point to the seizure-onset area, though they are less specific and sensitive than sVEEG and MRI. Preoperative neuropsychological testing is also useful for establishing a cognitive baseline, so as to measure change postoperatively.<sup>21</sup> Functional imaging includes interictal and ictal single photon emission computed tomography (SPECT) (which measures blood changes between and during a seizure, respectively), positron emission tomography (PET) (which measures metabolism changes between seizures) and functional MRI (which maps areas of normal brain function).<sup>22,23</sup> The functional imaging study is selected based on the patient's individual circumstances. MEG is an emerging technology that measures changes in the brain's magnetic field, in contrast to EEG, which measures electrical current generated by changes in the brain's electrical field.<sup>23,24</sup> The current detected by scalp electrodes is significantly attenuated and distorted by cerebrospinal fluid, dura, skull and scalp, which lie between the scalp and the cortical surface. In contrast, these tissues do not affect the magnetic field, whereas recorded magnetic field distributions reflect more accurately the cortical surface activity. Owing to the physical properties of electrical and magnetic fields, MEG detects current flowing tangentially (parallel to the cortex) but is insensitive to current oriented radially (from deep to the cortex). MEG is typically employed to localize interictal epileptiform discharges and serves as a useful adjunct to EEG, helping to customize the placement of intracranial electrodes for iVEEG recording. MEG is limited in its ability to record ictal events because the head position in relationship to the magnetic sensor has to be firmly fixed, which tends to be compromised by the movement during a seizure. MEG installations are costly, approximately \$3 to \$5 million. Finally, prior to the performance of epilepsy surgery an

intracarotid amytal (Wada) test is usually performed<sup>25,26</sup> to assess the lateralization of language and memory, so the surgeon can avoid harm to these important functions. The EEG is usually monitored during the procedure to assess the unilaterally dominant changes with delta and fast activities, and duration of the amytal effect, and screen for any seizure activity that might affect the interpretation of the results.

Often, the noninvasive evaluation will yield sufficient localizing information on which to base a decision to proceed with epilepsy surgery. However, in those cases when the noninvasive information is sufficiently discordant or ambiguous, iVEEG monitoring should be considered. Indications for proceeding to iVEEG include<sup>27,28</sup>

- Nonlocalizing ictal scalp EEG onset, with or without localizing lesion on imaging.
- Apparently bilateral ictal scalp EEG onset.
- Rapid propagation of seizures from one side to the other.
- Discordant ictal scalp EEG onset and imaging lesion (e.g., mesial temporal sclerosis on MRI and apparent frontal lobe EEG onset).
- Apparent extratemporal (e.g., frontal lobe) ictal scalp EEG onset.
- Concordance between imaging lesion and ictal scalp EEG onset, but presence of other confounding information such as prominent interictal epileptiform discharges elsewhere, cognitive deficit on neuropsychological testing from the area of proposed resection, or intracarotid amytal test suggesting preserved memory function in the area of a proposed resection.

### **THE ROLE OF THE EPILEPSY SURGERY CASE CONFERENCE**

The noninvasive presurgical evaluation accumulates a large amount of data that are sometimes in conflict or discordance, resulting in an unclear surgical plan. Since the principal goal of epilepsy surgery is to safely render the patient seizure free (or in some cases, to significantly reduce seizures) and the potential risks of neurosurgery are not trivial, it is extremely valuable to present the information before a multidisciplinary team of specialists who can deliberate on the findings and form a consensus plan. The epilepsy surgery case conference serves this function, promoting collaboration among epileptologists, epilepsy neurosurgeons, EEG physicians and technologists, neuropsychologists, radiologists, and psychiatrists. The group serves to maximize outcome and reduce risk to the patient in this high-stakes algorithm. Once advised of the recommendations of the collaborative team, the ultimate decision to proceed with iVEEG then rests with the patient.

### **THE EPILEPSY-MONITORING UNIT: CONSIDERATIONS FOR PERFORMING INVASIVE VIDEO EEG**

The purpose of an epilepsy-monitoring unit (EMU) is to safely and effectively record, review and store video EEG data. This is accomplished through a system that combines highly trained EEG technologists, a skilled electroencephalographer/epileptologist and nursing personnel in a space that promotes patient safety and workflow efficiency utilizing an infrastructure of advanced information technology.<sup>29</sup>

### **PERSONNEL**

The training, experience, and collaboration of the EMU personnel are critical. The EMU is typically directed by a physician (usually a neurologist) with subspecialty training in EEG, video EEG, and epilepsy. EEG technologists are responsible for the integrity of the video EEG recording and can play an important role in patient safety, data review, and storage. From a technologist's point of view, one key difference between the EEG laboratory and the EMU is that, in the latter, seizures are much more frequently recorded, and patient safety is at a premium. Because the technologist will spend a considerable amount of time with the patient, maintaining good rapport is important. The EMU should also be staffed by a complement of epilepsy-trained specialist nurses, with a staffing number adequate to provide safe and effective care to the patients, dependent upon the size of the EMU and the complexity of its patients. Beyond the primary concern of safety, the EMU nursing staff can also greatly aid in the diagnosis and localization of seizures by performing protocol-driven response (memory, language, motor function) testing during a seizure.

### **SPACE CONSIDERATIONS**

The EMU is usually housed within an acute-care hospital with access to all the inpatient services otherwise available to hospitalized patients. Adequate space must be devoted to the EMU, including rooms for the patients, the technical and nursing staff, and the recording and review equipment. The patient rooms should be well lit and easily accessible to nursing staff and EEG technologists, allowing for rapid access in the event of a seizure. Communication between the recording and patient rooms can be accomplished through a two-way intercom system. Video cameras should be positioned to provide a full-body view of the patient, with pan-zoom-tilt functions to react to patient movements (e.g., from bed to bedside chair).

### **SAFETY**

Safety considerations for carrying out iVEEG are identical to those described in Chapter 8, with an added degree of complexity owing to the postoperative and invasively instrumented condition of the patients. Seizure alarms (see "Computer Algorithms" below) and video monitors for the nurses are vital, as is some degree of ongoing human surveillance of the recording. This can be carried out by round-the-clock personnel (technicians, medical assistants, or EEG technologists), trained to maintain the ongoing recording and alert the nursing and physician staff to the presence of seizures accelerating in frequency or duration, or ongoing seizure activity (e.g., status epilepticus) that may pose a risk to the patient. Systems also exist to allow for the remote review of video EEG by the physician staff. Safety protocols should be in place in the event of alteration in the patient's condition. For example, a protocol may specify the conditions under which to administer a medication such as lorazepam to a patient experiencing an escalation in seizure severity or duration. A sound safety plan will have multiple redundant layers of security designed to minimize harm to the patient, regarding the unique characteristics of the EMU's patient population, physical space, personnel, and technology.

## THE TECHNIQUE OF INVASIVE VIDEO EEG

### RECORDING

#### *Electrodes and Placement*

Intracranial electrodes are placed according to the findings of the noninvasive evaluation and are designed to test the hypothesis about seizure onset. For example, if the suspicion is that seizures either arise from the right frontal or temporal lobe, electrodes will be placed primarily in these areas. If the presumption is that seizures arise from one or the other of the temporal lobes, electrodes will be placed around both temporal lobes. Prior to placement, selection of electrode location is critical because, unlike in sVEEG, coverage of the entire cortical surface is technically impossible. Also, once placed, iVEEG electrodes can only be moved or replaced through another operation. iVEEG electrodes are made of a flexible silicone-plastic elastomer material with imbedded platinum or stainless steel electrode contacts, typically spaced 1 cm apart. In order to tailor placement to the individual patient, electrodes come in a number of shapes and sizes (Fig. 9-2). These subdural electrodes consist of strip and grid electrodes. Strip electrodes are, as the name implies, a single row of recording contacts, longer than they are wide. They are most useful for reaching around areas of the cortical surface, such as the inferior or anterior temporal lobes, the poles of the frontal lobe, or the cortex deep in the interhemispheric fissure. Grid electrodes occupy a greater expanse of two-dimensional space and are primarily shaped as squares and rectangles, though sometimes as circles or semicircles. They are most useful for covering larger areas of exposed cortex, such as over the surfaces of the frontal or temporal lobes, or for placement over a lesion. Strip and grid electrodes are designed to sit on the brain surface in the subdural space. Depth electrodes consist of contacts spaced along a flexible shaft and are introduced into the brain tissue to access deeper structures inaccessible by subdural electrodes, such as the mesial frontal or temporal lobes. Examples of strip, grid, and depth electrodes are shown in Figure 9-3A to C. Subdural and depth electrodes serve different functions, the former to record from the cortical surface and the latter to record from deeper structures. They are often used in tandem in a given

patient, and can provide complementary information.<sup>30-32</sup> Stereo-electroencephalography, the technique of modeling the seizure-onset zone through three-dimensional analysis of EEG signals from a combination of surface and depth electrodes, may be particularly useful in MRI-negative (nonlesional) cases.<sup>33</sup> Studies have shown the use of depth electrodes to be as safe as subdural electrodes.<sup>32-34</sup>

#### *Recording Methods*

iVEEG should be recorded with a sufficiently high sampling rate to satisfy the Nyquist theorem, which states that the sampling rate must be at least twice the maximal frequency of activity of interest in order to avoid loss or aliasing of the signal (see *Practical Guide: EEG*, Chapter 4, Fig. 4-5). Some advocate sampling at rates as high as 2,000 Hz, and 200 Hz should be considered the absolute minimum so as not to exclude recording of faster frequency activity. Large-capacity computer systems are required to make such recordings. Given the volume of data recorded and stored, and ongoing advances in computer technology, an EMU must make a perpetual commitment to equipment upgrades through a capital equipment plan.

#### *Induction of Seizures*

Seizures are a fundamentally unpredictable phenomenon, yet iVEEG cannot be recorded in a given patient indefinitely (unless fever intervenes, patients can be recorded for as long as 2–3 weeks, but, usually no longer) and steps are usually taken to increase the chance of a seizure. These methods typically include withdrawal of anticonvulsant medication and sleep deprivation, though the utility of each has not been formally proven in the iVEEG setting.<sup>35</sup> Since iVEEG is recorded only in patients with partial (focal)-onset seizures, activating procedures such as hyperventilation and photic stimulation are of no value. In the days following electrode implantation, patients occasionally undergo a quiescent period of reduced seizure frequency. A recording plan longer than several days should be the norm, although occasional patients will have sufficiently frequent seizures so that the recording can be stopped within several days. In most cases, relevant data sufficient to form a surgical plan are usually gained within 7 to 10 days,<sup>36</sup> though the planned timeframe should be open-ended enough to accommodate patient-to-patient differences.

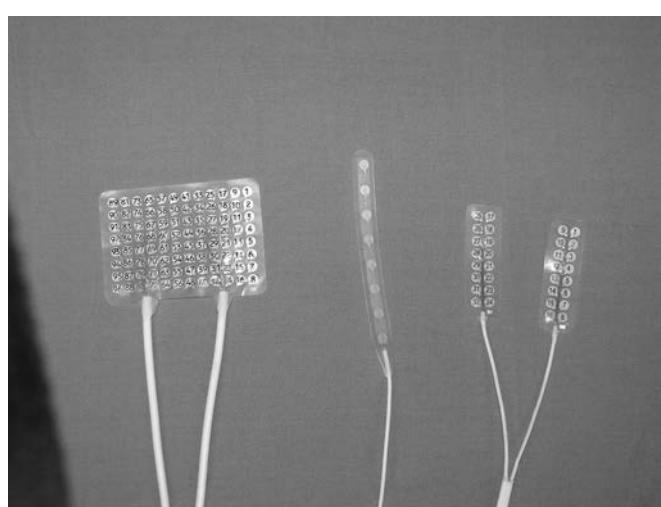
### DATA STORAGE

The patient undergoing iVEEG assumes certain risks and expects an optimal likelihood of a favorable surgical outcome. iVEEG data are therefore critical and irreplaceable. Redundancy in data storage should be the norm, utilizing some combination of high-fidelity backup systems such as Redundant Array on Independent Disks and a network backbone. Depending on the capacity, protocols, and needs of the EMU, offsite storage may also be desirable to protect the data from an on-site calamity and to facilitate physician review.

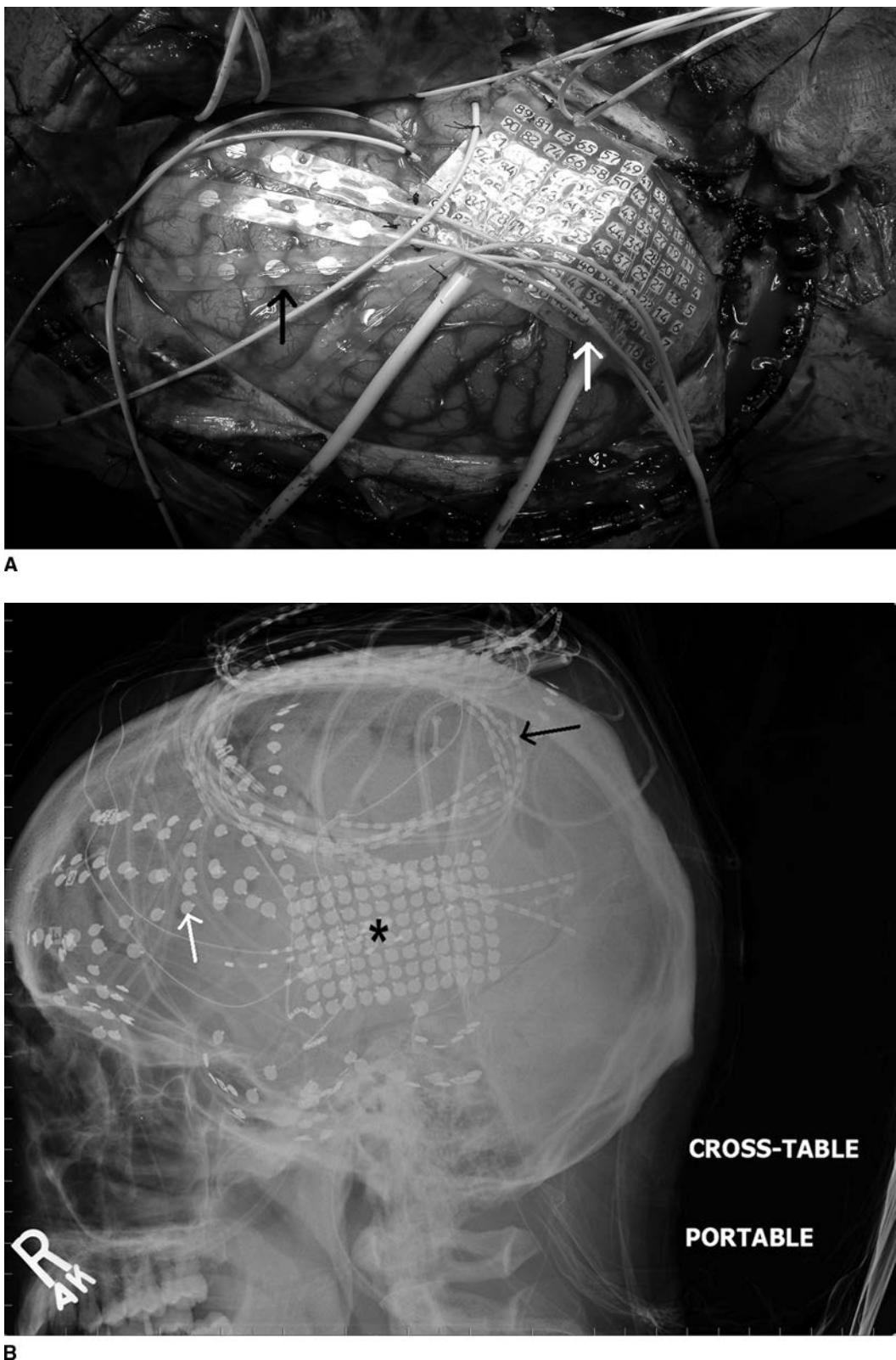
### REVIEW

#### *Visual Inspection of iVEEG*

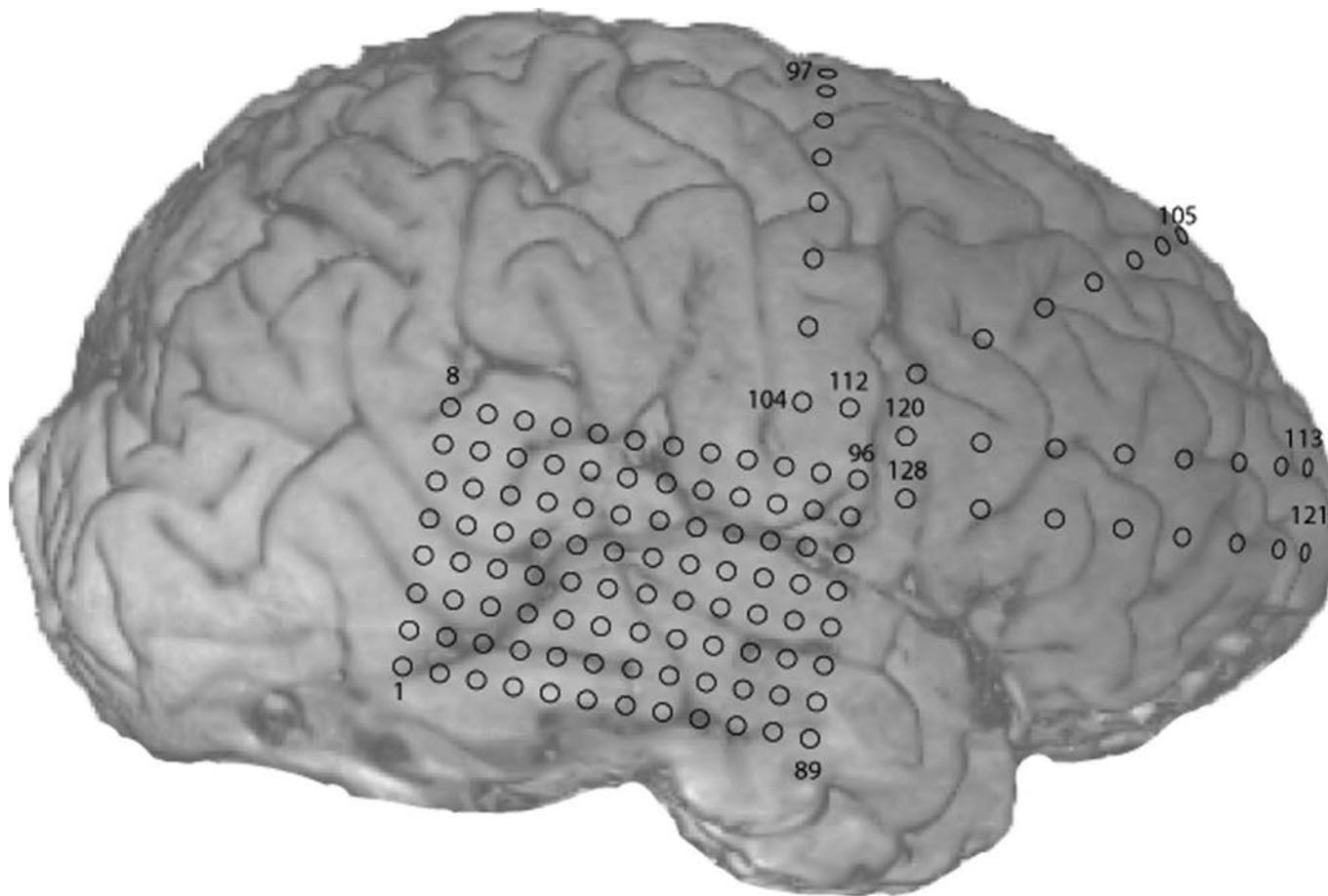
As noted above, iVEEG is tailored to the individual patient with respect to the extent and location of electrode placement.



**Figure 9-2.** Examples of strip and grid electrodes.



**Figure 9-3.** Placement of invasive EEG electrodes. **A:** Intraoperative photograph, showing grid (white arrow) and strip (dark arrow) placed on the brain surface in the subdural space. **B:** Postoperative lateral radiograph showing electrode placement (grid electrodes indicated by asterisk and strip electrodes indicated by white arrow) and connecting wires (dark arrow). **C:** Image fusing the three-dimensional rendering of the patient's MRI scan with electrode placement. Numbers indicate corners (grid) and ends (strip) of electrodes.

**C****Figure 9-3. Cont'd.**

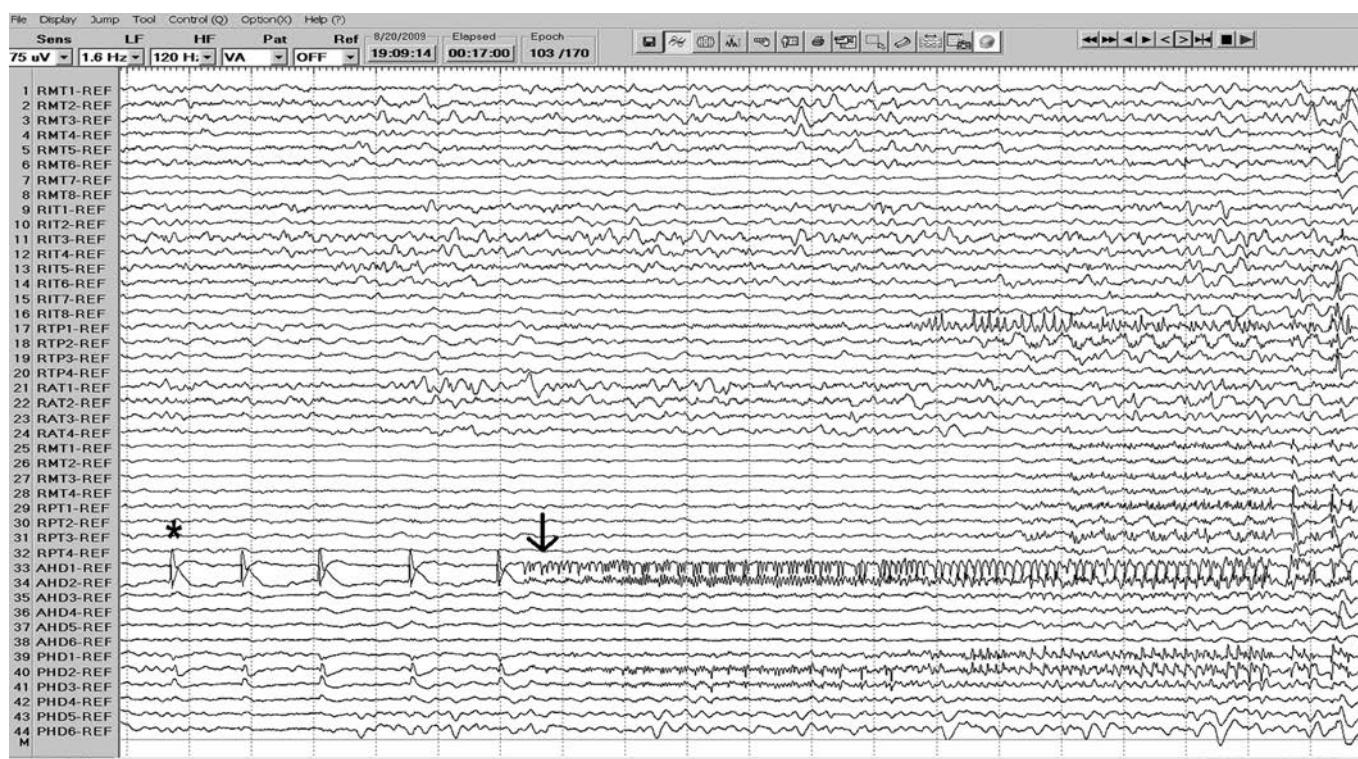
The review montage will, therefore, be customized for each patient and the reviewing physician will take some time to conceptualize (and perhaps even map out) the montage before commencing review. iVEEG can be reviewed using either a bipolar or a referential montage, the latter often utilizing an intracranial electrode remote from the suspected ictal-onset zone or a reference electrode placed in the subgaleal space. An image uniting the patient's structural imaging with electrode locations, usually provided by the imaging or surgical team, can prove helpful in iVEEG interpretation. The goal of review is to detect background, interictal and ictal changes that determine the localization of the patient's seizures, and to use these data to form the basis for a surgical resection plan.

Changes in background activity are of less predictive value in iVEEG than they are in routine EEG or sVEEG, but areas of persistent slowing can indicate cerebral dysfunction. The interictal recording will frequently show a much greater number and distribution of interictal epileptiform discharges than the scalp EEG, due to the proximity of the recording electrodes to spike source generators and elimination of signal attenuation from dura, skull and scalp (see *Practical Guide: EEG*, Chapter 5, Fig. 5-36).

Interictal epileptiform discharges of traditional morphology (sharp waves, spikes) may have equivocal bearing on seizure localization, and a surgical decision should not be based primarily on background activity or interictal discharges. On the other hand, high-frequency oscillations (HFOs) may be an

important predictor of seizure-onset.<sup>37,38</sup> Ripples (80–250 Hz) and fast ripples (250–500 Hz) of 50 to 150 ms duration can be recorded from mesial temporal structures and the latter have been shown to correlate with the seizure onset zone.<sup>39–41</sup> Recording of these discharges requires a high sampling rate (at least 1,000 Hz), and adjustment of the standard sensitivity, filter and page display parameters. HFOs tend to be revealed when the review bandwidth is raised above that of standard review (band-pass of ~50–500 Hz). The display gain should be increased so as to expand the EEG recording in the vertical axis, and 1 to 2 seconds per computer screen reviewed.

The primary goal of iVEEG monitoring is the recording and interpretation of the patient's habitual seizures. As a general rule, the faster the ictal frequency at onset, and the more restricted the discharge, the more confident one can be that the actual onset of the seizure has been recorded. Sometimes, however, ictal activity can propagate rapidly throughout recording contacts, even to recording contacts that are physically remote from the contacts of origin.<sup>42,43</sup> An example of seizure onset and propagation is shown in Figure 9-4. One great advantage of digital video EEG recording is that it allows for post hoc alterations in page display, montage, filter settings, and gain. The seasoned iVEEG reviewer will use changes in these parameters on a case-by-case basis to most accurately determine location of seizure onset. Seizures that rapidly propagate beyond their focus of onset tend to yield a lower seizure-free outcome



**Figure 9-4.** Focal seizure onset recorded via invasive EEG electrodes. Clinical onset (arrow) accompanies localized fast ictal EEG activity maximal from mesial contacts of the right temporal lobe depth electrodes, preceded by several seconds of repetitive spike activity (asterisk). (AHD, right anterior hippocampus depth; PHD, right posterior hippocampus depth; RAT, right anterior subtemporal strip; RIT, right inferior-lateral temporal strip; RMT, right middle subtemporal strip; RPT, right posterior subtemporal strip; RTP, right temporal pole strip. Sensitivity: 75  $\mu$ V/mm; low-frequency filter: 1.6 Hz; high-frequency filter: 120 Hz; page display: 20 seconds.)

following epilepsy surgery.<sup>42</sup> An important caveat to interpretation is that seizure onset can only be directly discerned from the electrodes actually placed in the patient's head. Since iVEEG monitoring does not involve holocranial electrode placement as in sVEEG there are, by its nature, large areas of the brain from which there is no recording. This may sometimes yield ambiguous or falsely localizing information, as when a seizure occurs but no ictal EEG change is seen at clinical onset (clinical onset preceding EEG change indicates that the seizure has started somewhere, whether the EEG onset is seen or not). Likewise, seizures that display diffuse, poorly localized EEG change at onset should raise the suspicion that the seizure is arising from an area not being recorded (Fig. 9-5A and B), and may warrant adjustment of electrode placement or termination of the study without tissue resection.

Review is aided by ongoing computer detection of interictal and ictal discharges. The EEG technologist can also add great value by previewing the recording for the physician, essentially adding an additional layer of review to avoid missing important data. Monitor technicians or EEG technologists can also watch the recording in real time, further reducing the likelihood of missing a critical event.

### Computer Algorithms

Computer algorithms are employed to scan the ongoing data in real time and annotate changes that might indicate interictal or ictal discharges for further review. Varieties of such seizure and spike detection applications have been reported in the literature

and are commercially available.<sup>44–47</sup> First-generation algorithms monitored the ongoing EEG signal for changes in amplitude, frequency, and rhythmicity. Second-generation algorithms use artificial neural networks and a “learning” process to detect change from an individual patient's baseline, or recognize user-identified patterns of interest. With such applications, a trade-off often has to be made between sensitivity (detecting *all* seizures and seizure-like patterns) and specificity (detecting *only* seizures), and they therefore augment rather than replace human EEG review.<sup>48</sup> Judicious use of a spike-and-seizure detection algorithm can aid to reduce the amount of EEG data to be reviewed. In iVEEG, detecting seizures is usually more useful than detecting interictal discharges, so the detection parameters will need to be adjusted accordingly.

### The Role of Video

The video recording provides important complementary information and should be considered an independent and necessary component of iVEEG recording. Video review can be especially helpful for:

1. Monitoring patient safety and alerting staff to the presence of a seizure that requires intervention.
2. Correlating clinical and EEG onset. Clinical onset that precedes EEG onset raises the suspicion of a remote (unrecorded) onset.
3. Determining if an event is of clinical significance, or sub-clinical.

4. Determining if an event represents one of the patient's habitual seizures, or a distinctly different sort of event (and therefore should not be used to base a surgical decision).
5. Providing lateralizing and localizing clues.

Other than bathroom breaks, all efforts should be made to keep the patient on full-camera view throughout the iEEG study.

### Functional Testing

Prior to electrode removal and the performance of epilepsy surgery, it is common to perform electrical cortical stimulation testing of eloquent cortical areas of the brain serving language, motor and sensory functions, especially if resection may involve one or more of these areas. The goal is to avoid inadvertent resection of the normal functioning cortex. Cortical stimulation is performed by delivering pulses of electrical activity through the recording electrodes and clinically testing impairment of eloquent functions such as speech, movement, and sensation.<sup>49,50</sup> Cortical stimulation occasionally produces sustained epileptiform activity known as an after-discharge, a possible indication of irritable cortex and a potential, though not primary, clue to seizure onset.<sup>51,52</sup> Cortical electrical stimulation may also produce a frank seizure, but caution must be used in integrating these induced seizures into the surgical plan, particularly if they differ clinically from the patient's habitual seizures.

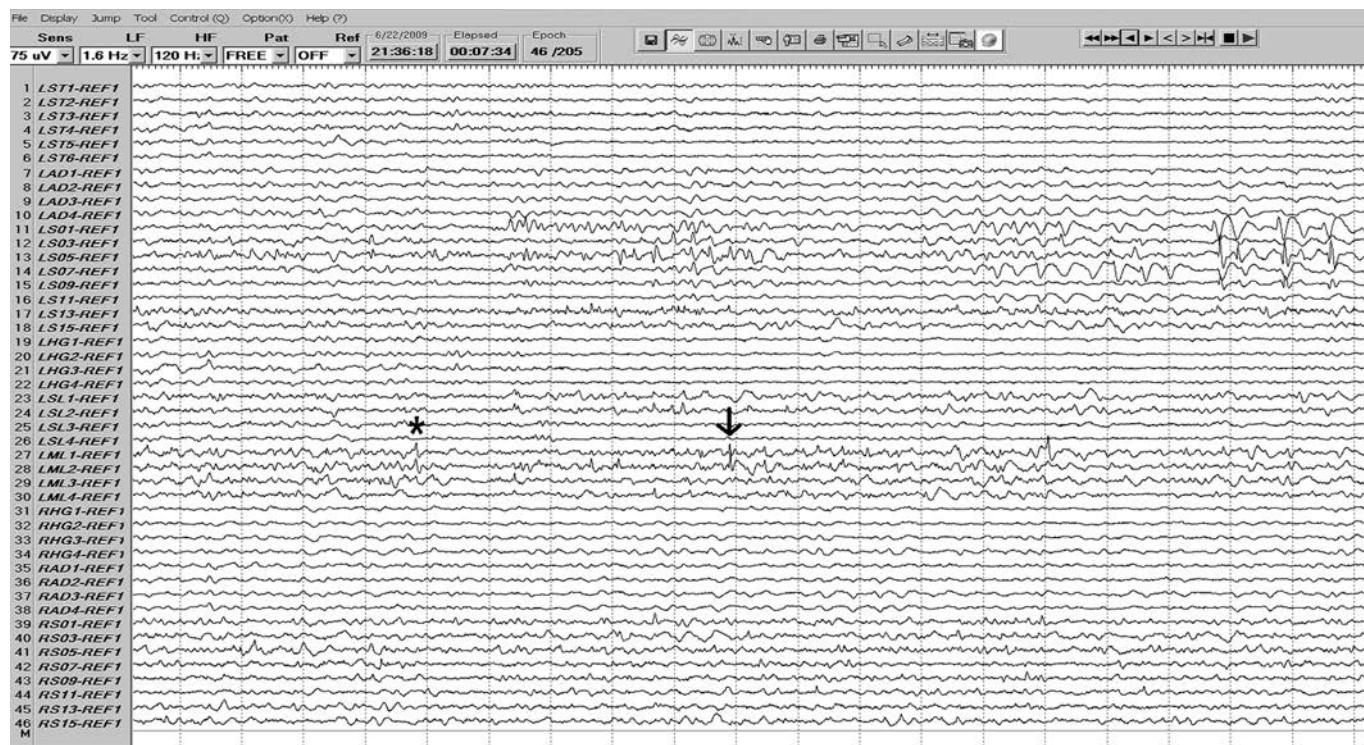
### Human Brain Research

Direct access to the human brain over days to weeks provides a unique and highly valuable opportunity to study basic properties

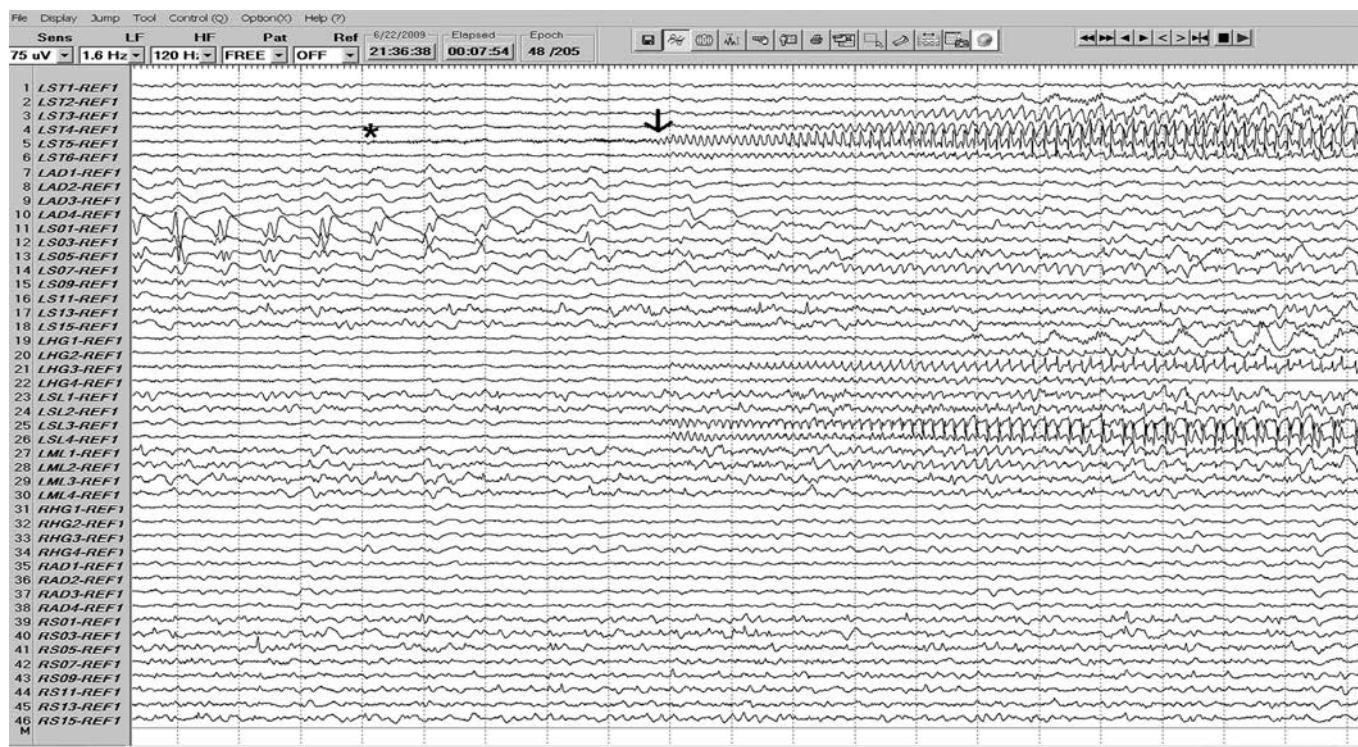
of neurons and their networks. Techniques such as microelectrode<sup>53,54</sup> and microdialysis<sup>55</sup> recording have helped shed light on many fundamental properties of cognition, motor control, sensation and emotion, and may one day lead to the development of computer-brain interfaces by which neuronal activity is used to drive robotic or prosthetic devices.<sup>56</sup> Research recording devices can be combined with clinical EEG electrodes to permit simultaneous recording, while placing the patient at no additional risk. A drawback of this technique is that, by definition, recordings are being made from abnormal (epileptic) brain, allowing, at best, extrapolation to normal brain conditions. Still, with many hours to pass between seizures, epilepsy patients are usually highly willing and robust research candidates. A full discussion of research methods is beyond the scope of this chapter, but the interested reader is directed to several comprehensive reviews<sup>57–60</sup> with extensive references.

## OUTCOME MEASUREMENTS

The primary outcome goals of epilepsy surgery are to significantly or completely reduce seizure frequency (optimal efficacy) without causing additional harm to the patient (optimal safety). If seizures are found to arise unilaterally from one mesial temporal lobe, an anterior temporal lobectomy or one of its variations tends to yield seizure freedom in 60% to 80% of cases.<sup>14,27,28,61,62</sup> Among the remaining 20% to 40% of patients, most have their seizures significantly reduced. Better outcome is predicted if seizures do not propagate outside the hippocampus in less than 5 seconds<sup>63</sup> of onset and if the operative pathology reveals



**Figure 9-5.** Ambiguous seizure onset recorded via invasive EEG electrodes. **A:** Irregular spikes (asterisk) maximal at contacts LML 1 and 2 preceded by several seconds clinical onset (arrow). Repetitive spikes from the LS strip follow.

**B**

**Figure 9-5. Cont'd. B:** (immediately follows **A**) shows fast activity from LS contact 5 (*asterisk*), followed by evolving ictal activity from this and surrounding contacts (*arrow*). (LAD, left amygdala depth; LHG, left Heschl's gyrus depth; LML, left middle lateral temporal strip; LS, left subtemporal grid; LSL, left superior-lateral temporal grid; LST, left superior temporal gyrus depth; RAD, right amygdala depth; RHG, right Heschl's gyrus depth; RS, right subtemporal grid. Sensitivity: 75  $\mu$ V/mm; low-frequency filter: 1.6 Hz; high-frequency filter: 120 Hz; page display: 20 seconds.)

hippocampal sclerosis or gliosis.<sup>61</sup> In some cases, such as when epileptiform activity is expressed independently from both temporal lobes, temporal lobectomy may be considered more palliative than curative, with a greater chance of reducing seizures than of achieving actual seizure freedom.<sup>64,65</sup> When seizures arise outside the temporal lobe, seizure-free outcome varies from about 25% to 50%.<sup>62,64</sup> Better outcome of extratemporal seizures is predicted by presence of a lesion on MRI.<sup>66</sup> Poorer outcome is seen with diffuse or multifocal seizure onset<sup>66,67</sup> However, in appropriately selected patients the chance of postoperative seizure control may still be significantly greater than with further medication trials or therapy with vagus nerve stimulation (VNS).

iVEEG carries with it a small risk of complications, including infection, hematoma, and permanent new neurologic deficit, each seen in less than 3% of patients.<sup>37</sup> These risks, and the further small risk of surgical resection, must be weighed against the risks of ongoing, poorly controlled seizures.

Performance of iVEEG is not a commitment to ultimate surgical resection, and a small percentage of patients undergoing iVEEG will prove to have insufficiently localizing seizures on which to base a successful resection strategy.<sup>27,36,63</sup> If iVEEG does not reveal a resectable seizure focus, electrode removal is carried out without resection. Such patients are candidates for further medication trials or VNS.<sup>68</sup> Other quality-of-life-based outcome measures, as addressed in Chapter 8, are not fundamentally different in patients who reach resection through iVEEG, compared to those who have resection following noninvasive testing.

Epilepsy surgery is typically followed by observation in the hospital for at least several days, followed by a period of

convalescence at home. During this time, postoperative complications such as headache, fever, and new neurologic deficits should be reported promptly to the surgical team. The epilepsy team should be alerted to the occurrence of postoperative seizures, especially if different from the habitual preoperative seizures. As noted above, recurrence of habitual seizures is expected in a certain percentage of patients, and may warrant a medication adjustment. Onset of a new sort of seizure may herald the presence of an operative lesion of note (e.g., a hematoma) that may call for imaging, or may represent postoperative nonepileptic phenomena such as panic attacks or pseudoseizures. An additional round of sVEEG may be required for diagnosis. Depressed mood occasionally develops in the weeks following resection, and tends to respond promptly to medication. Gradual reduction of antiepileptic medication can be considered several months following surgery, though the epileptologist should guide this process and carefully advise the patient of the risk of seizure recurrence.

## CONCLUDING REMARKS

iVEEG monitoring is an important means to achieving seizure freedom in a subset of patients undergoing evaluation for epilepsy surgery. This is generally indicated when the noninvasive testing fails to sufficiently localize seizure onset and, owing to its inherent risk, is strictly reserved for those patients serious about pursuing surgical resection. It is carried out under controlled nursing, technical, and physician supervision. A high-quality

recording, followed by careful review and storage of the data, is performed using modern computer networking technology. Following successful epilepsy surgery, patients can enjoy significant seizure control and improvement in quality of life.

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# Long-Term Bedside EEG Monitoring for Acutely Ill Patients (LTM/cEEG)

## INTRODUCTION

The recent advancement of computer technology has allowed continuous EEG (cEEG) recording at the patient's bed side. This has become possible because of increased memory size, fast processing speed, and also improved resolution of the video screen. Continuous and long-term monitoring (LTM) of EEG allows the evaluation of dynamic changes of brain function that may not be visible by clinical examination alone. With accumulation of LTM data in the intensive care unit (ICU), it became apparent that non-convulsive seizures (NCSZs) are relatively common in acutely ill comatose or stuporous patients. Because of the lack of motor manifestation, NCSZ can easily be overlooked without LTM EEG recording. And, because of the intermittent and unpredictable occurrence of NCSZ, a single 20 to 30 minute routine EEG recording would miss capturing these seizures. The value of LTM EEG has been further strengthened by concomitant video recording, networking capability, ability of storing large amounts of data for many hours (>24 hours), and also by the automatic computer analyses of seizure/spike detection and power spectrum measurement.

## INDICATION FOR LTM

The most common reason for LTM EEG is to find out if the patient is having nonconvulsive status epilepticus (NCSE) or intermittent episodes of NCSZ in the acutely ill comatose or obtunded patients. The following clinical conditions raise the question of NCSE or NSCZ.

- The expected recovery does not occur after brain surgery.
- The patient does not gain consciousness after head trauma.
- Consciousness remains impaired with paucity of positive physical finding or lack of radiological examination.
- There is fluctuating mental status without explainable cause.
- Unexplainable comatose or obtunded state.
- There is no recovery after convulsive status epilepticus or single seizure.

Other justifiable reasons for performing LTM EEG include episodes of seizure-like symptoms such as muscle twitching, body posturing, eye deviation, chewing, pupillary abnormalities, or autonomic symptoms, but without overt convolution.<sup>1-3</sup> The LTM EEG may also be indicated for evaluation of vasospasms or cerebral ischemia, especially after subarachnoid hemorrhage (SAH) or interventional neuroradiological procedure. The LTM EEG may be also used for the evaluation of progressively changing brain function, either worsening or improving, that is, prognostication. The LTM EEG is also used for therapeutic guidance in maintaining a burst suppression pattern with barbiturates or other anesthetic/sedative drugs or electrocerebral silence by therapeutic hypothermia.

## INCIDENCE OF NCSE OR NCSZ IN THE ICU

NCSZ is defined as an electrographic seizure without clinical signs such as face or limb twitching, eye deviation, nystagmus, pupillary changes or autonomic changes (respiration, EKG, sweating, etc.). NCSE is when NCSZs occur continuously or near continuously lasting more than 30 minutes.<sup>4,5</sup> The overall incidence of NCSZ or NCSE in patients who are in coma or unexplained altered mental status in ICU settings (inclusive of pediatric patients) varies from about 10% to 40%.<sup>6-9</sup> Of various etiologies, the post convulsive status epileptics have the highest incidence of NCSZ or NCSE; one study showed close to half the patients who had convulsive status epileptics developed NCSZ (14% of these were NCSE) after the convulsions had stopped.<sup>10</sup>

The next most common etiology for NCSZ is post anoxic cerebral insult, ranging from 35% to 42%.<sup>6,8,11,12</sup> During cardiac arrest associated with aortic surgery, and for neuroprotective measures, the EEG can be made therapeutically "flat" by use of hypothermia. Cerebral ischemia may occur following this hypothermia and NCSE may occur during the re-warming period.<sup>12</sup> The NCSZ associated with ischemic brain injury carries a grave prognosis.<sup>13</sup>

The third most common etiology is toxic-metabolic encephalopathy ranging from 5% to 25%.<sup>5,6,8,14</sup> These include uremia, hypertensive encephalopathy, drug intoxication or withdrawal, hepatic failure, hypo- and hyperglycemia.

NCSZ are fairly common in patients with postoperative brain surgery,<sup>15–17</sup> traumatic brain injury,<sup>18–20</sup> intracerebral hemorrhage,<sup>21–23</sup> ischemic stroke,<sup>21,23,24</sup> and SAH.<sup>3,25,26</sup> The incidence of NCSZ in these conditions varies, ranging from 5% to 20%. NCSZ and NCSE are also common in neonates, infants, and children in NICU (neonatal ICU) or PICU (pediatric ICU); one study showed 44% of patients who underwent ICU monitoring had NCSZ and 75% of these were NCSE.<sup>7</sup> The common etiologies are a history of epilepsy, ischemic brain injury, and stroke.<sup>27–29</sup>

It is expected that the incidence of capturing seizures (either clinical or nonconvulsive) would be higher with LTM EEG than with the routine 30 minutes of recording in the ICU setting. One study showed that, of 105 ICU patients, seizures were recorded in 11% within the first 30 minutes of recording and increased to 27% by prolonging the EEG to a mean of 2.9 days.<sup>30</sup> The incidence of capturing the first seizure within 24 hours of LTM EEG was higher in noncomatose than in comatose patients.<sup>31</sup>

## RECORDING OF LTM

The electrodes used for LTM EEG are the same as used in routine EEG (silver-silver chloride or gold). They are attached most securely by collodion. Because the EEG is recorded without the attendance of a technologist most of the time, it is important that the electrodes are attached securely enough for many hours of recording. In some cases extra or redundant electrodes may be placed. This is especially true for the “system” or “common” reference that can be placed anywhere on the scalp. In digital EEG recording, if the system reference is lost, the entire recording will be lost. Thus at least two system reference electrodes should be used; as long as one of the system references is working, the recording will not be affected.

In addition to EEG electrodes, EKG electrodes should always be placed because abnormal EKG can mimic epileptiform activity (see *Practical Guide: EEG*, pp. 284–286, Fig. 14-14). EKG can also sometimes provide important clues for cardiac related spells. Other electrodes may include EMG over appropriate muscles, especially when the patient shows muscle twitches or rhythmic contractions. Because these patients often undergo MRI or CT scanning during the monitoring session, the electrodes must be removed and replaced after the examination is done. This is a nuisance and is time consuming for technologists. MRI-compatible or CT scan-compatible electrodes have now become commercially available. Subdermal needle electrodes are acceptable for comatose patients and may be preferentially used for patients with skin problems or for patients who have fresh surgical wounds on the scalp. Needle electrodes have lower impedance than disc electrodes which is advantageous for reducing electrical interference artifacts in the electrically hostile ICU environment. In some cases, pulse oxymetry or intracranial pressure monitoring can be useful and is accomplished by adding DC amplifiers.<sup>32</sup>

Using a covering or wrapping over the entire set of electrodes may help to minimize accidental dislodging of the electrodes. The electrode wires should be bundled together and placed away from other instruments and at a distance from the patient's

reach. Even if the patient is immobile, physicians or other ICU personnel may move the head or body without consideration of the attached EEG wires.

In addition to the EEG, video recording with audio helps to identify seizure versus artifacts from various activities in the ICU. EEG activity mimicking seizure patterns can be created by chewing, rhythmic massage, patting, rhythmic chest percussion, shaking, rubbing, tremors, etc. (see *Practical Guide: EEG*, Chapter 14). Also, the audio allows recognition if the patient is given alerting stimuli intentionally or unintentionally. It is not uncommon to see increased epileptiform discharges with arousals, either spontaneous or by external stimulation (see Fig. 10-5).<sup>33</sup> This may be recognized by increased muscle artifact but can also be verified by reviewing the video with audio. The video screen is usually set up at the patient's bed side, but may be accessed at the nursing station and a remote reading room.

LTM EEGs are recorded in the electrically “noisy” ICU environment where many electrical instruments are attached to the patient and many people are working around the patient's bed side. Low electrode impedance and secure grounding minimize the contamination of electrical interference. If high-frequency noise cannot be eliminated, a lower high-frequency filter may be used, but one should be cautious in EEG interpretation since lowering the high-frequency filter, for example, from 70 to 15 Hz may change the appearance of muscle or movement artifacts to look like spike discharges (see *Practical Guide: EEG*, Chapter 14, Figs. 14-38 and 14-39).

With the start of EEG monitoring, the technologist should test the patient's responsiveness by calling his name or asking questions. If there is no response, the technologist delivers stimulation starting by touch and if there is no response to that, the stimulus intensity is gradually increased to painful stimulus (nail bed pressure or sternum rub). The technologist should check the integrity of the recording at least twice daily. If the patient has some type of spell, the technologist should ask the nurse, medical staff, or family member to mark the events, with a push button marker that registers on the EEG recording. ICU nursing staff may be able to write the time of the event and describe the clinical features of the event in the medical record. The technologist also needs to pay attention to medication changes, especially anticonvulsants, anesthetics, and sedative drugs or muscle relaxants.

If the recording continues more than several days, check the skin and scalp conditions for the presence of irritation or “break down.” If present, the primary physician and/or electroencephalographer should be alerted and appropriate measures should be taken. It is possible to continue the EEG recording by slightly displacing the electrode locations, but this should be clearly documented.

Commercially available EEG instruments are now capable of transmitting EEG data with video on line to remote sites through the internet. Thus, EEG information can be accessed anytime and anywhere. As long as the patient's confidentiality is kept secure (according to HIPPA regulations), this is an extremely convenient and important advancement for the EEG technologist, electroencephalographer, and referring physician. The electroencephalographer can periodically check the evolution of EEG change, if any, and the technologist can check the integrity of the EEG recording throughout the day as needed at a remote site. Remote access also allows sending the EEG

data with video from a local community hospital to major medical centers where expert electroencephalographers or epileptologists are available for consultation to provide prompt and appropriate evaluation and treatment to the patient.

Successful LTM EEG and appropriate management for the patient are based on close communication among the referring physician, nursing staff, electroencephalographer, and technologist.

## DURATION OF LTM

A very common question is how long the EEG recording should be continued. Generally, noncomatose patients tend to show their first seizure earlier than comatose patients. One study found that 95% of the noncomatose patients had their first seizure within 24 hours, and it was 85% for comatose patients (from 110 patients with seizures detected during LTM EEG).<sup>31</sup> It is therefore possible that a 24-hour LTM EEG may be sufficient for capturing a seizure for a noncomatose patient but not for comatose patients. Although no data are available, overall if there is no interictal or ictal EEG pattern for 3 days, it is reasonable to terminate the monitoring.

## EVALUATION OF LTM

The evaluation of interictal and ictal patterns is essentially the same as with routine EEG (see *Practical Guide: EEG*, Chapter 10), but distinction between ictal and interictal or nonictal patterns is not always clear. When frequent spike or spike-wave discharges occur in a random sequence, they are likely of the interictal pattern. Episodes of progressively changing patterns in frequency and amplitude or rhythmic wave forms are likely ictal events. The most difficult case is deciding between NCSE and metabolic encephalopathy such as hepatic encephalopathy when a more or less continuous rhythmic or periodic sharp-delta triphasic wave occurs. It was once thought that the triphasic waves abolished by short-acting benzodiazepines were ictal discharges, but it is now known that the triphasic waves associated with metabolic encephalopathy can also be abolished by benzodiazepine;<sup>34</sup> thus, this does not help to distinguish between the two. If, however, the patient shows clinical improvement, it is likely NCSE. In general, the triphasic waves of ictal patterns show a more “spiky” configuration than the triphasic waves of metabolic origin, therefore finding the “spike” is important to distinguish them.

Another situation where it is difficult to distinguish ictal versus interictal patterns is periodic lateralized epileptiform discharges (PLEDs). Most PLEDs are interictal or post ictal patterns and, therefore it is important to find the ictal event using LTM for at least a few days (see *Practical Guide: EEG*, Chapter 10, Fig. 10-36, see also Fig. 10-3 in this chapter). Some PLEDs are clearly ictal when associated with focal limb jerking, which is time locked to the discharges (epilepsia partialis continua).

## SEIZURE AND SPIKE DETECTION USING COMPUTER SOFTWARE

Page-by-page review of LTM EEG is time consuming for the electroencephalographer. In order to reduce vast amounts of

EEG data to be reviewed, automatic seizure or spike detection computer programs are commercially available. Despite much improvement and sophistication of computer technology in recent years, spike or seizure detection programs are far from perfect. The computer detects muscle activity or various artifacts as spikes and any rhythmic activity (such as sinusoidal and rhythmic alpha or sleep spindles or any rhythmic artifact) can be detected as a seizure (ictal) event. In reality more than 90% of the computer-detected spikes or ictal events are false-positive detections. The computer is still not capable of complex analyses of wave forms, spatial distribution, and temporal factors of a given wave or pattern that skilled electroencephalographers can instantaneously recognize and differentiate seizure/spike versus artifacts. Despite significant deficit, the seizure and spike detection program is useful by reducing the amount of data to be reviewed by allowing the computer to detect abundant false-positive data. One should also be aware of false-negative results; the computer will likely miss electro-decremental seizure or short-lasting or less rhythmic ictal discharges.

## THE ASSESSMENT OF PROGRESS FOR ACUTE CEREBRAL DYSFUNCTION

The LTM EEG can be utilized not only for finding episodic events such as seizure, but also for assessing the progress of acutely injured brain function and its prognostication during the course of illness. LTM EEG showing reactivity to external stimulation, spontaneous change, episodic sleep patterns, or a progressive decrease of slow waves replaced by faster frequency activity suggests a favorable prognosis. The prognosis is unfavorable if LTM EEG shows relentless and monotonous patterns without reactivity or variability.<sup>35-37</sup> EEG is especially sensitive to cerebral ischemia, which shows a decrease of fast (beta) activity and increase of delta slow waves. This occurs when cerebral blood flow is below 18 to 25 mL/100 g/min (see Chapter 6).<sup>38,39</sup> LTM EEG is often used during the acute phase of SAH because vasospasm occurs in 50% to 70% of patients after SAH.<sup>40</sup> The vasospasms tend to occur within 3 to 14 days after the onset of SAH and cause cerebral ischemia or infarction in close to 50% of patients.<sup>41</sup> Because prompt treatment can prevent cerebral infarction or ischemia, early detection of these events is important. The vasospasms can be detected by transcranial Doppler or angiography but these tests evaluate the vascular state only at the time of examination. LTM EEG reflects brain function continuously and is useful for the timely detection of EEG changes when vasospasm occurs. The EEG worsening can be reflected by increased slow waves, either by diffuse or focal pattern.<sup>42,43</sup> EEG may also help to evaluate the effectiveness of treatment.

Using quantitative EEG (qEEG) analyses, various algorithms have been introduced to automatically detect the deterioration or improvement of EEG activity after SAH. The EEG deterioration due to vasospasms was detected by the reduction of total spectral power,<sup>44</sup> decrease in variability of alpha frequency power,<sup>43</sup> or reduction of alpha/delta frequency power ratio after stimulation.<sup>42</sup>

The ischemic infarction can be detected by Brain Symmetry Index based on the difference of mean spectral power of 1 to 25 Hz between the left and right hemispheres.<sup>45</sup>

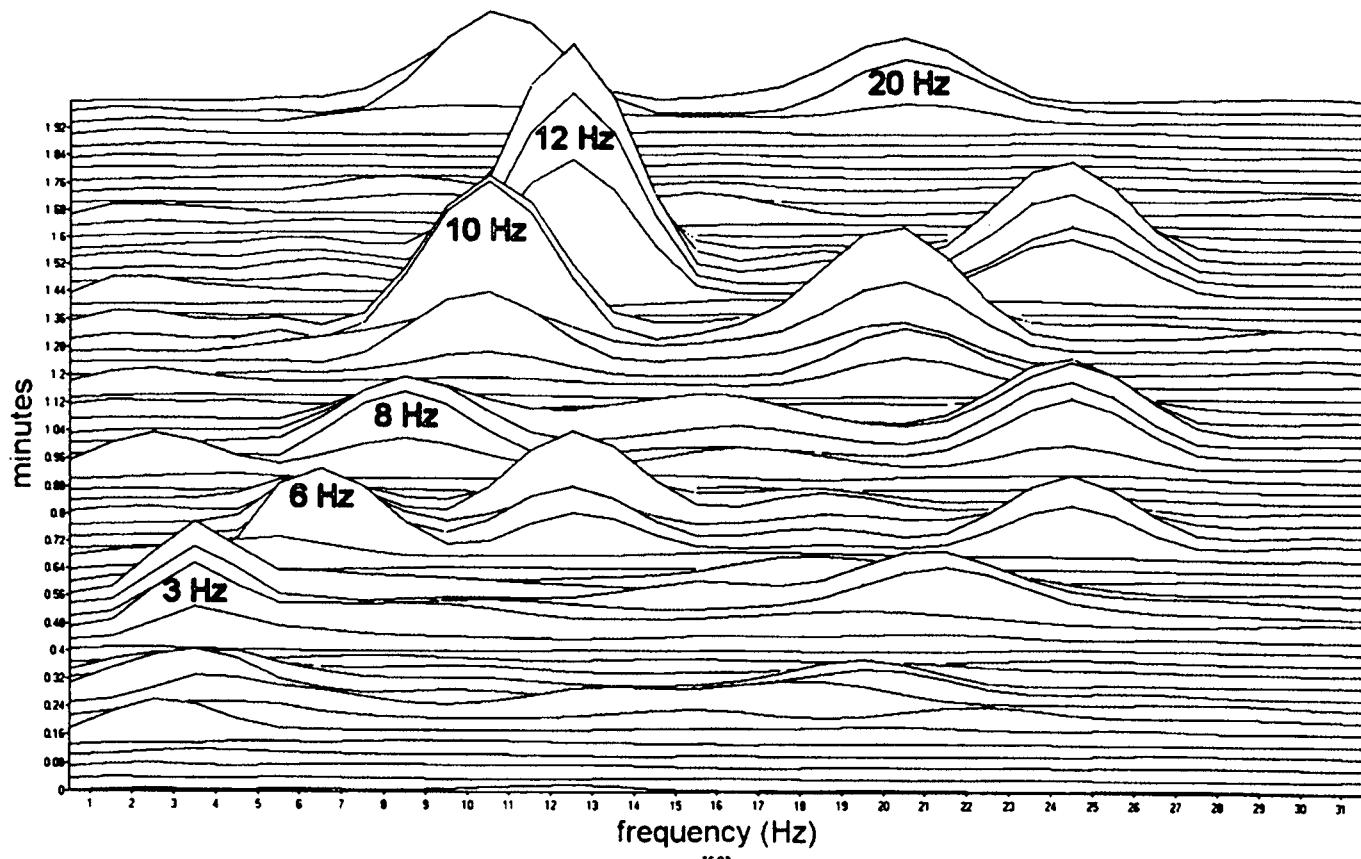
## THE USE OF QUANTITATIVE EEG ANALYSES FOR LTM

The standard visual analysis requires considerable amount of time even by skilled electroencephalographers to review the entire 24 hour EEG. In addition to the spike or electrographic seizure detection program, quantitative analyses using spectral power by Fourier transformation helps to identify transient or gradual changes of the power spectrum during LTM EEG. If qEEG is performed appropriately, the data and figures created by qEEG can be screened by personnel who are not familiar with EEG. The qEEG is also useful even for experienced electroencephalographers who could miss the slow and gradual trends of EEG changes when relying only on visual inspection (see Fig. 10-6). However, because qEEG cannot differentiate various artifacts from genuine EEG activity, one should never rely solely on the qEEG without correlating original EEG data. Therefore, final interpretation of the LTM EEG still relies on the skilled electroencephalographer.

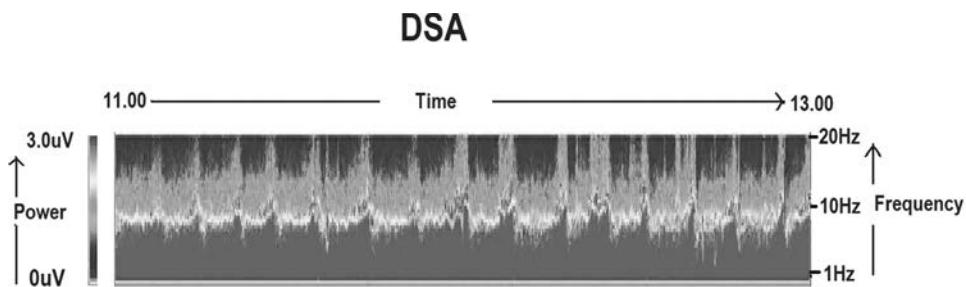
The commonly used qEEGs are compressed spectral array (CSA) and density spectral array (DSA). CSA is created by plotting the frequency values along the *x*-axis and successive

epochs (time) along the *y*-axis. The amplitude of spectral power is then expressed by the height of vertical deflection which gives three-dimensional effects (Fig. 10-1). DSA is expressed by depicting the spectral power amplitude by a gray scale or color differences with time on the *x*-axis and frequency values on the *y*-axis (Fig. 10-2). In creating CSA or DSA, it is possible to select any single electrode or multiple electrodes, or combinations of all electrodes from the left and/or right hemisphere. The DSA is often combined with spectral edge frequency (SEF), which stands for the frequency below a certain percentage (usually 85%–95%) of the total power of a given signal location. For example, 85% SEF is the frequency in which 85% of the EEG spectrum power resides. The SEF is useful to see the shift of frequency in time (see Fig. 10-2). The time scale can also be changed; the shorter time scale allows more detailed analyses of short-lasting epochs but this may make it more difficult to recognize the gradual changes of the EEG pattern. The longer time scale reveals the event of gradually changing EEG patterns more clearly but short-lasting events may escape detection.

Other methods of qEEG include very simplified techniques such as amplitude integrated EEG in which a simple calculation



**Figure 10-1.** An example of CSA display. The *x*-axis indicates frequency and the *y*-axis indicates time in minutes. The height of each tracing represents the amount of EEG power. This CSA was created by intermittent photic stimulation at 3, 6, 8, 10, 12, and 20 Hz stimulus rates. (From Scheuer MK, Wilson SB. Data analysis for continuous EEG monitoring in the ICU: seeing the forest and the trees. *J Clin Neurophysiol* 2004;21:353–378, with permission.)



**Figure 10-2.** An example of DSA display. The x-axis indicates time and the y-axis indicates frequency. The amount of EEG power is expressed by different colors with the highest power in red and the weakest power in blue. This shows power spectrum changes for 2 hours, revealing cyclic power alteration with increased power and frequency changes. The yellow zigzag line in this and subsequent figures represents SEF of 85% showing the frequency change along with power spectrum change. The rising line indicates increase of faster frequency activity. (See color insert.)

of rectified EEG amplitudes<sup>46</sup> to the highly sophisticated method using EEG bispectrum analysis which is a signal-processing technique that determines both EEG linear (frequency and power) and non-linear (phase and harmonic) components and quantitates the inter-frequency phase coupling of EEG signals.<sup>47</sup> Details of these are beyond the scope of this chapter.

Here, several cases of LTM in which DSA provided valuable information are presented.

**Case No. 1:** The patient was an 85-year-old man with multiple medical histories that included hypertension, type II diabetes mellitus, COPD, and obstructive sleep apnea. He was found unresponsive and observed to show intermittent episodes of head turning with rightward gaze preference and rigidity of the left arm. The EEG on admission, when the patient was comatose, showed PLEDs from the right hemisphere with frontal dominance (Fig. 10-3A). The DSA depicted from the right parasagittal electrodes showed rhythmic and cyclic changes of spectral power with approximately 5- to 10-minute intervals; the trough of the spectral power corresponded with the PLEDs and its peak corresponded to the ictal discharges with increased fast activity (Fig. 10-3B). The examination of the video showed that no apparent clinical seizure activity was associated with the ictal discharges. By counting the number of peaks, close to 40 seizures were recorded within 6 hours of the start. Further detailed evaluation of power spectrum changes showed that the power increased gradually, ultimately evolving to the ictal event, which was almost predictable. The trough of each cyclic event corresponded with the return of PLEDs pattern (Fig. 10-3C). The DSP became a stable pattern at 9 hours after the start of monitoring, implying no further ictal event, but PLEDs continued (Fig. 10-3D).

**Case No. 2:** The patient was an 80-year-old woman, with past histories of cardiomyopathy and hypothyroidism, who was found unconscious apparently after cardiac arrest. The patient was comatose when the initial EEG was obtained. The EEG showed bilaterally diffuse nearly periodic sharp/spike wave discharges with intervals of 1 to 1½ seconds (Fig. 10-4A). These periodic discharges were not continuous but intermittently faded away, replaced by burst suppression pattern, which

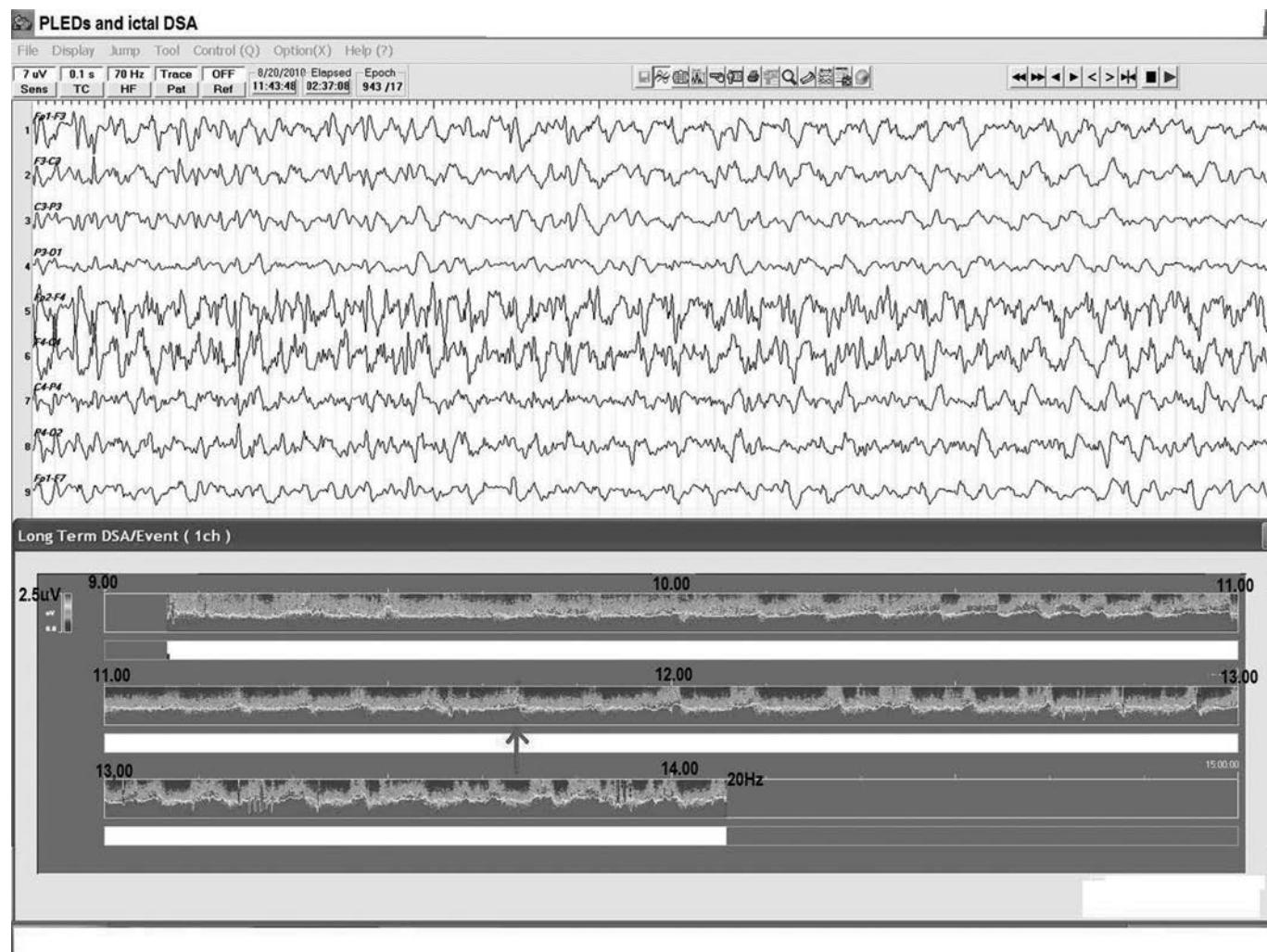
corresponded to a decrease of spectral power (Fig. 10-4B). After about 2 hours of recording, DSP started to show an episode of different power spectrum from the earlier recording exhibiting four discrete band paths with abrupt onset. These DSA changes corresponded with a sudden emergence of 6-Hz spike discharges involving primarily the right temporal region and their harmonic frequencies (12 and 18 Hz) in addition to the underlying delta frequency activity (Fig. 10-4C). These discharges occurred independently from diffuse and recurrent sharp/spike discharges. When 6-Hz spike discharges faded away, recurrent and diffuse sharp discharges remained (Fig. 10-4D). With some of these 6-Hz spike episodes, the video showed left arm twitching synchronous to the spike discharges, indicating that these were clinical as well as electrographic ictal events. The presence of harmonic activities implied that 6-Hz spike discharges had a fixed frequency without progressive changes or variability.

**Case No. 3:** The patient was a 48-year-old man who went into ventricular tachycardia in the emergency room while he was being evaluated for his chest pain. At the time of the EEG recording, the patient was comatose. The EEG showed diffuse and low-voltage delta with superimposed beta and alpha activities (Fig. 10-5A). The DSA showed fluctuating spectral power with intermittent increase of power lasting variable durations (Fig. 10-5B). These episodes of power increase were reflected by increased diffuse triphasic sharp/delta waves that were always associated with increased muscle tone. These occurred spontaneously or when the nurses were working with the patient which was verified by reviewing the video.

**Case No. 4:** The patient was a 75-year-old woman who was diagnosed with SAH (subarachnoid hemorrhage) after acute onset of headache and seizure. The EEG showed diffuse 5 to 6 Hz theta and low-voltage delta waves (Fig. 10-6A). The DSA revealed gradual increase of spectral power (Fig. 10-6B and C). These changes were reflected by the gradual increase of delta/theta amplitude and finally emergence of broad triphasic waves (Fig. 10-6D). Because these EEG changes were gradual and relatively subtle, their detection might have been missed using page-by-page mode of EEG without the help of DSA.



**Figure 10-3.** With the start of the monitoring at the time indicated by arrow, EEG showed right > left periodically recurring spike discharges (PLEDs) (A). The DSA of 6 hours' time span later showed cyclic power changes. The details of these cyclic changes are better viewed by expanding time scale to 2 hours per line (B), which revealed there was gradual increase of power and at the peak (indicated by arrow), EEG showed electrographic ictal discharges with recurrent polyspike-wave involving right frontal region. At the trough of power spectrum, EEG changed back to PLEDs pattern (C). About 9 hours after the start of LTM EEG, the cyclic changes of power spectrum became a stable pattern that corresponded with the continuous PLEDs pattern (D). (See color insert.)



**Figure 10-3. Cont'd.** (See color insert.)



C

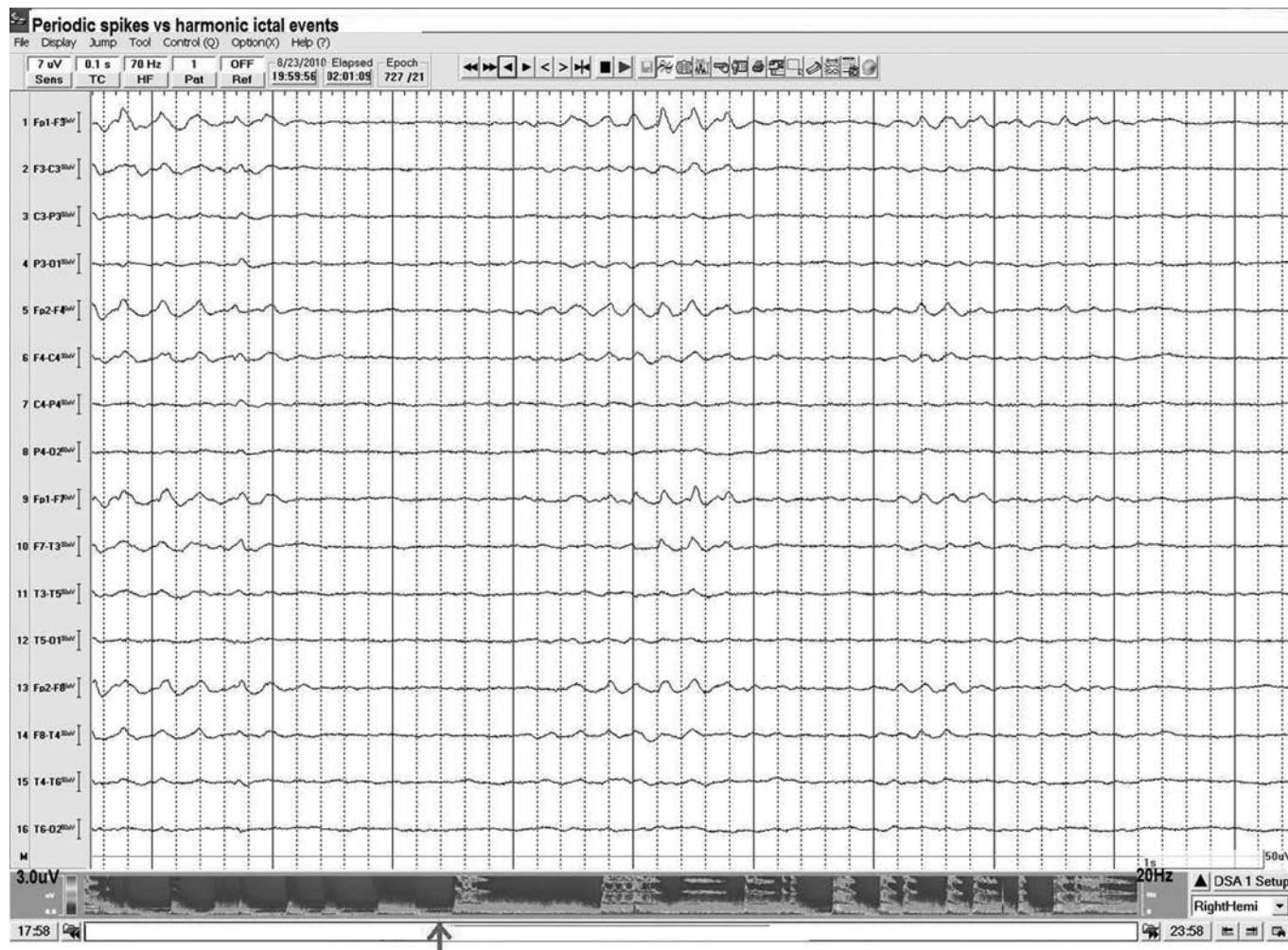
**Figure 10-3. Cont'd.** (See color insert.)



**Figure 10-3. Cont'd.** (See color insert.)

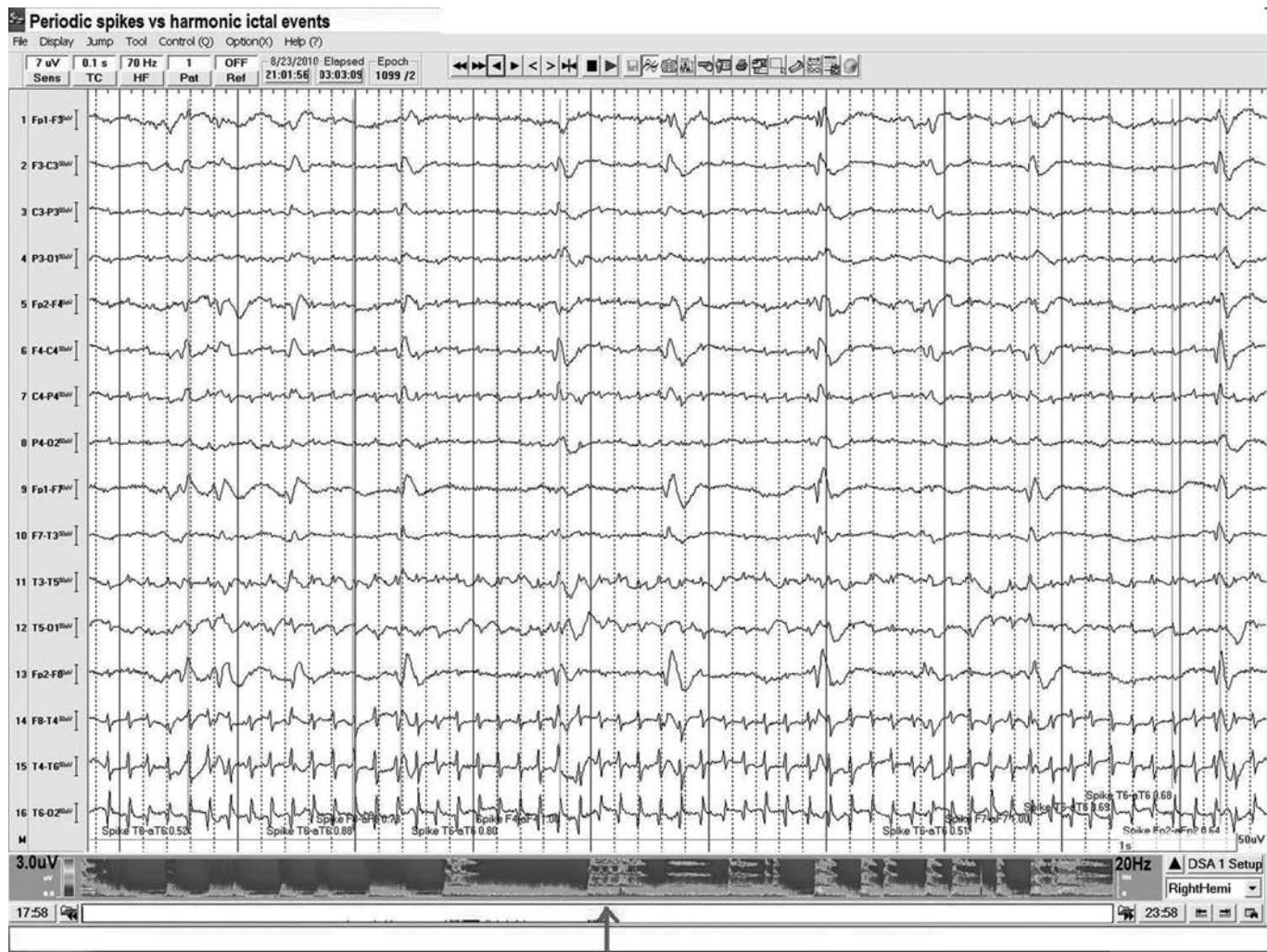
**A**

**Figure 10-4.** During early phase of monitoring, EEG showed episode of diffuse periodic sharp discharges coinciding with the increased slow wave power (indicated by *arrow mark*) (**A**; this and subsequent figures represent DSAs of 6 hours' time span). This was followed by the decreased power when EEG showed burst suppression pattern with 1 to 2 seconds theta bursts followed by suppression periods of 1 to 3 seconds (**B**). About 2 hours after the start of monitoring there were sudden changes in DSA profile showing three distinct frequency bands in addition to the delta band frequency. These three bands corresponded to sudden occurrence of 6-Hz spikes in the right temporal region spreading to the parasagittal electrodes that appeared independently from diffuse frontal dominant sharp and spike waves (**C**; EEG representing at *arrow mark*). Apparently 6-Hz spike discharges created additional harmonic responses at 12 and 18 Hz due to their consistent and fixed frequency throughout the event. The 6-Hz spike discharges gradually faded away (**D**; EEG representing at *arrow mark*). Note still remaining sporadic spikes shown in *oval circles*. These ictal episodes continued to recur in next 6 hours. These discharges were electrographic ictal events, some of which were associated with clinical seizures with left arm twitching corresponding to each spike. (See color insert.)



B

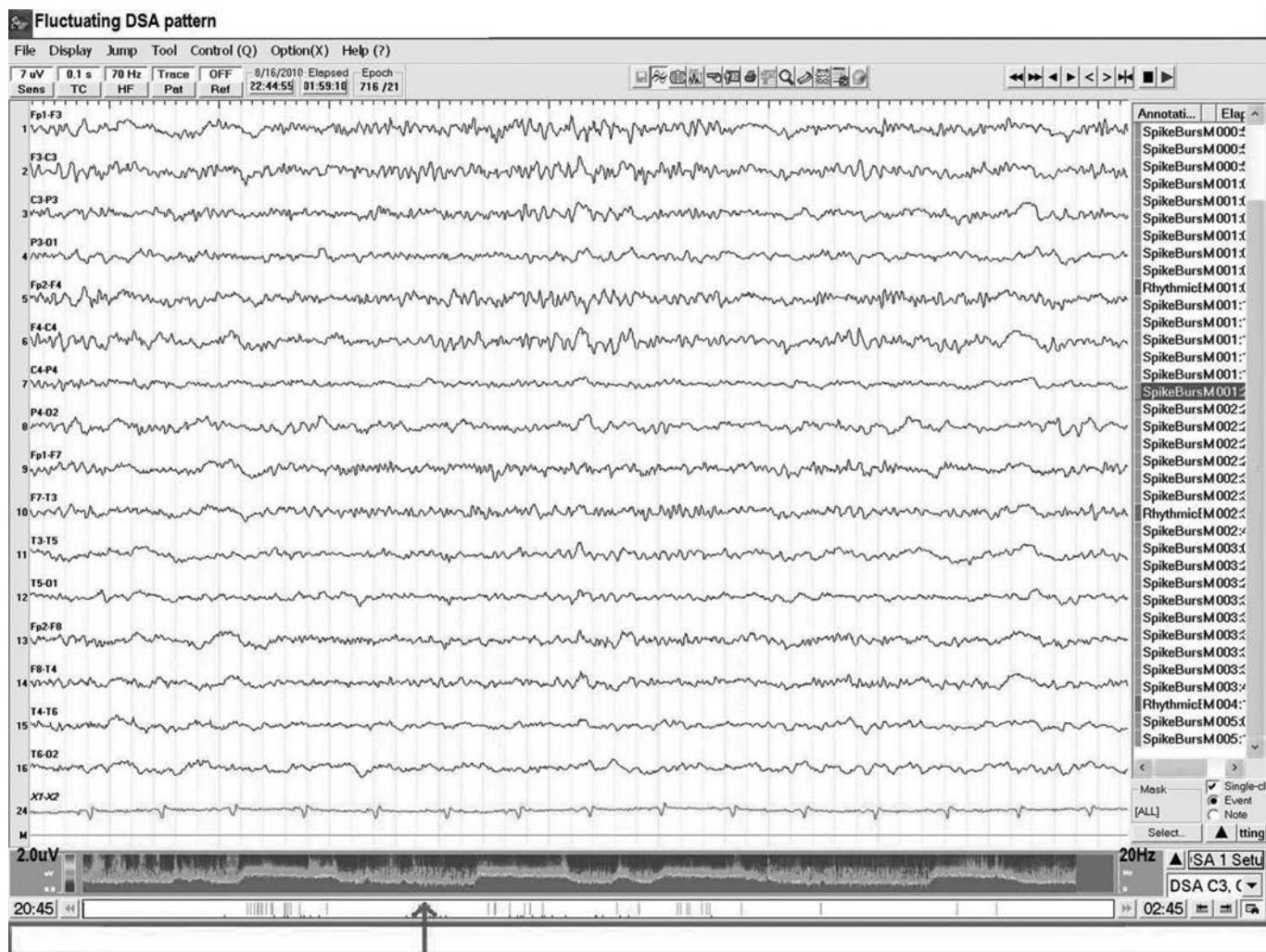
**Figure 10-4. Cont'd.** (See color insert.)



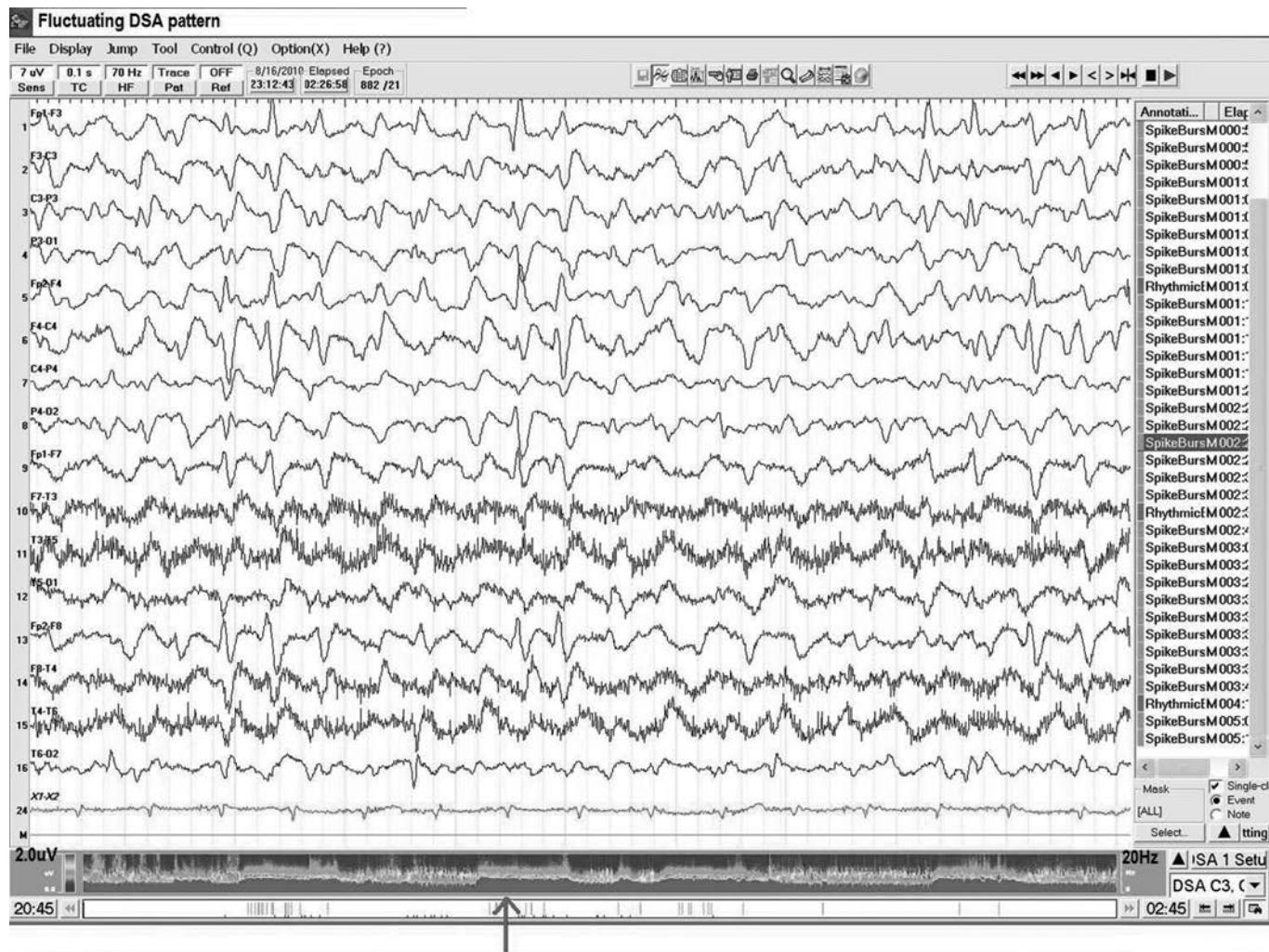
**Figure 10-4.** Cont'd. (See color insert.)



**Figure 10-4. Cont'd.** (See color insert.)

**A**

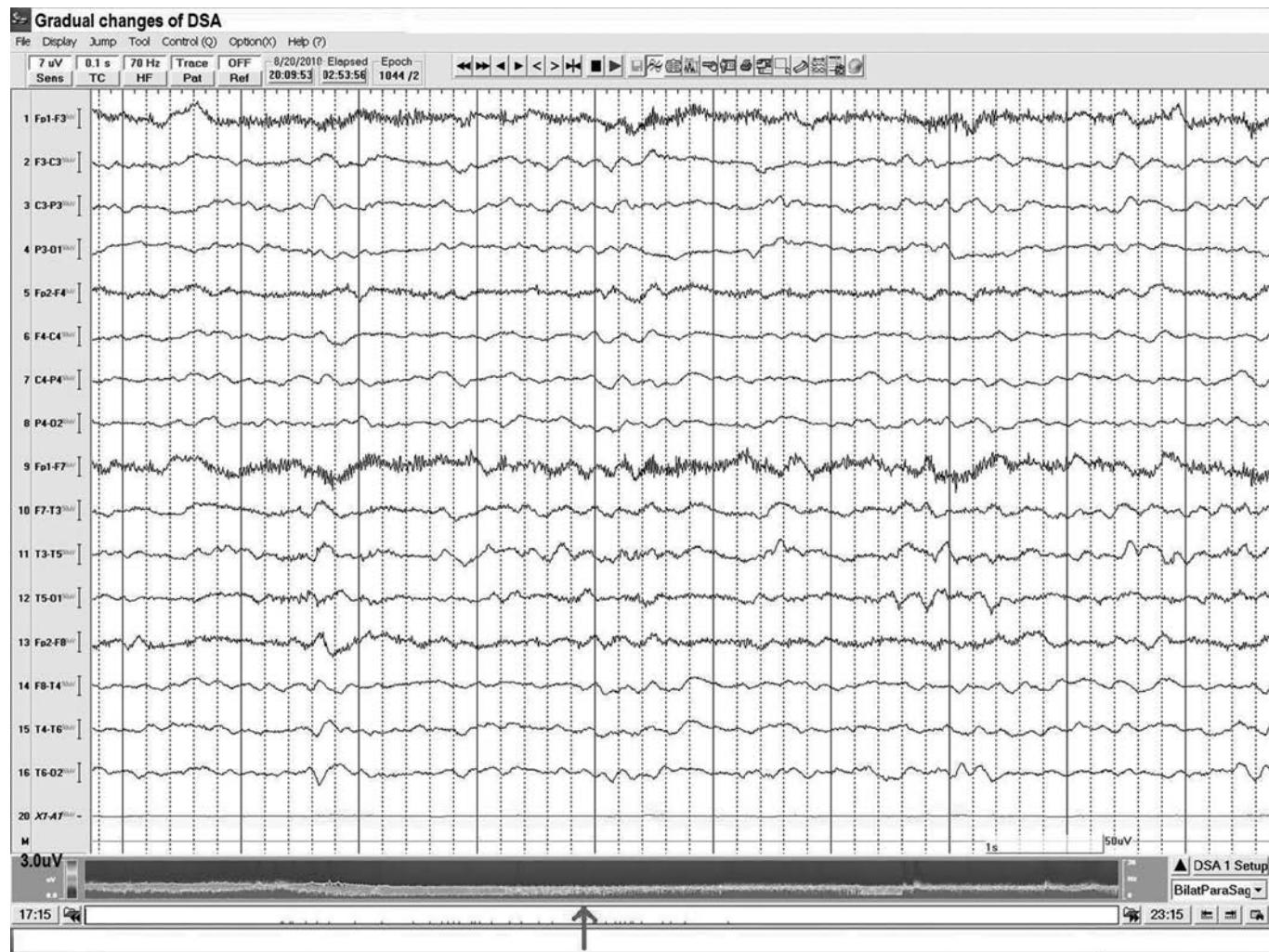
**Figure 10-5.** This 6 hour DSA showed fluctuating spectral power; at the time of low power (indicated by arrow), EEG showed bilaterally diffuse, relatively low-voltage delta activity with superimposed beta activity (**A**). Whenever the power increased (as in **B** at the arrow), EEG showed increased diffuse delta waves and intermittent triphasic sharp/delta paroxysmal discharges, which were always associated with the increased muscle tone. The review of the video confirmed that the triphasic paroxysmal discharges increased whenever the patient was aroused by family members or ICU personnel, or spontaneously. (See color insert.)

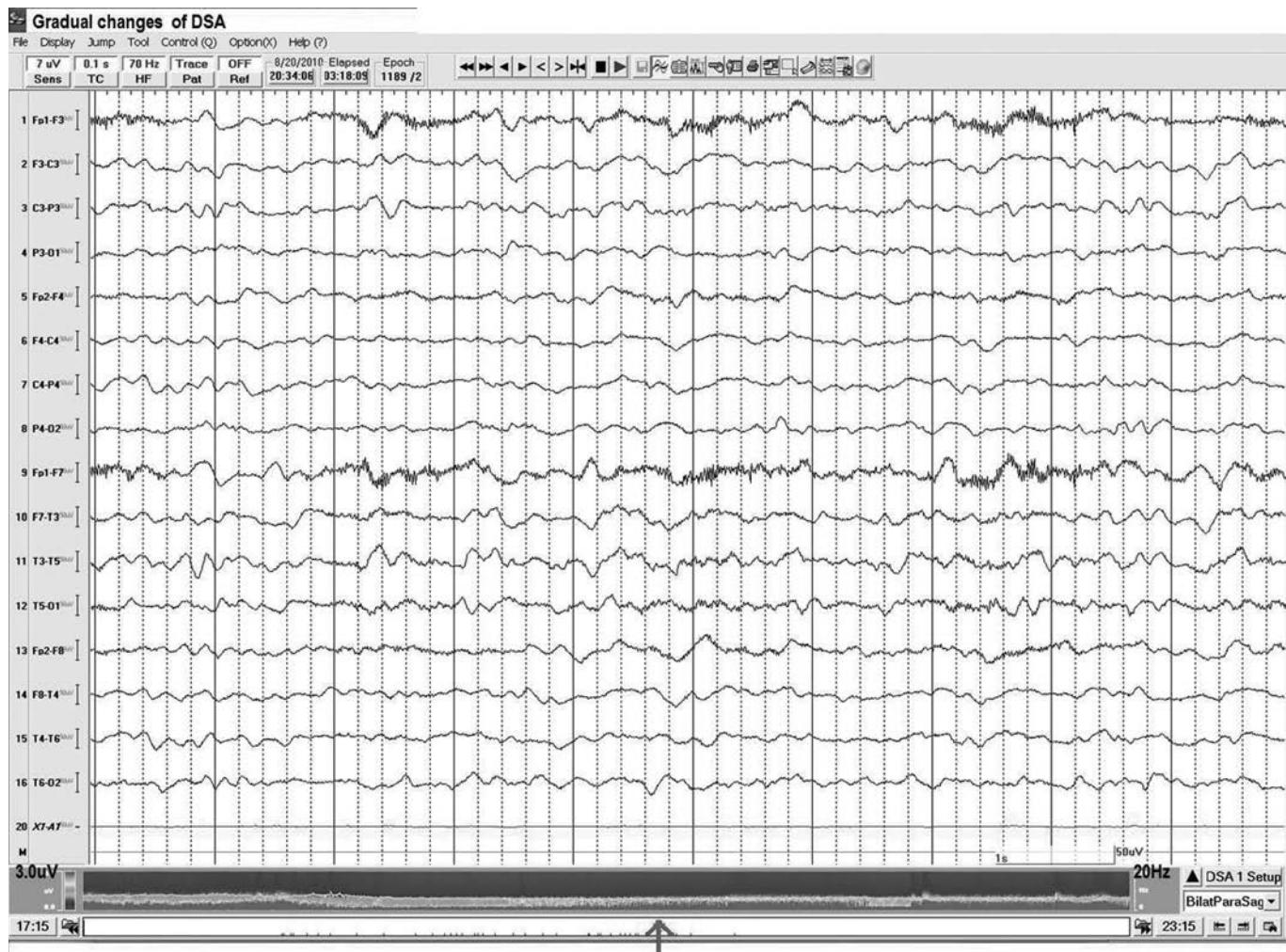


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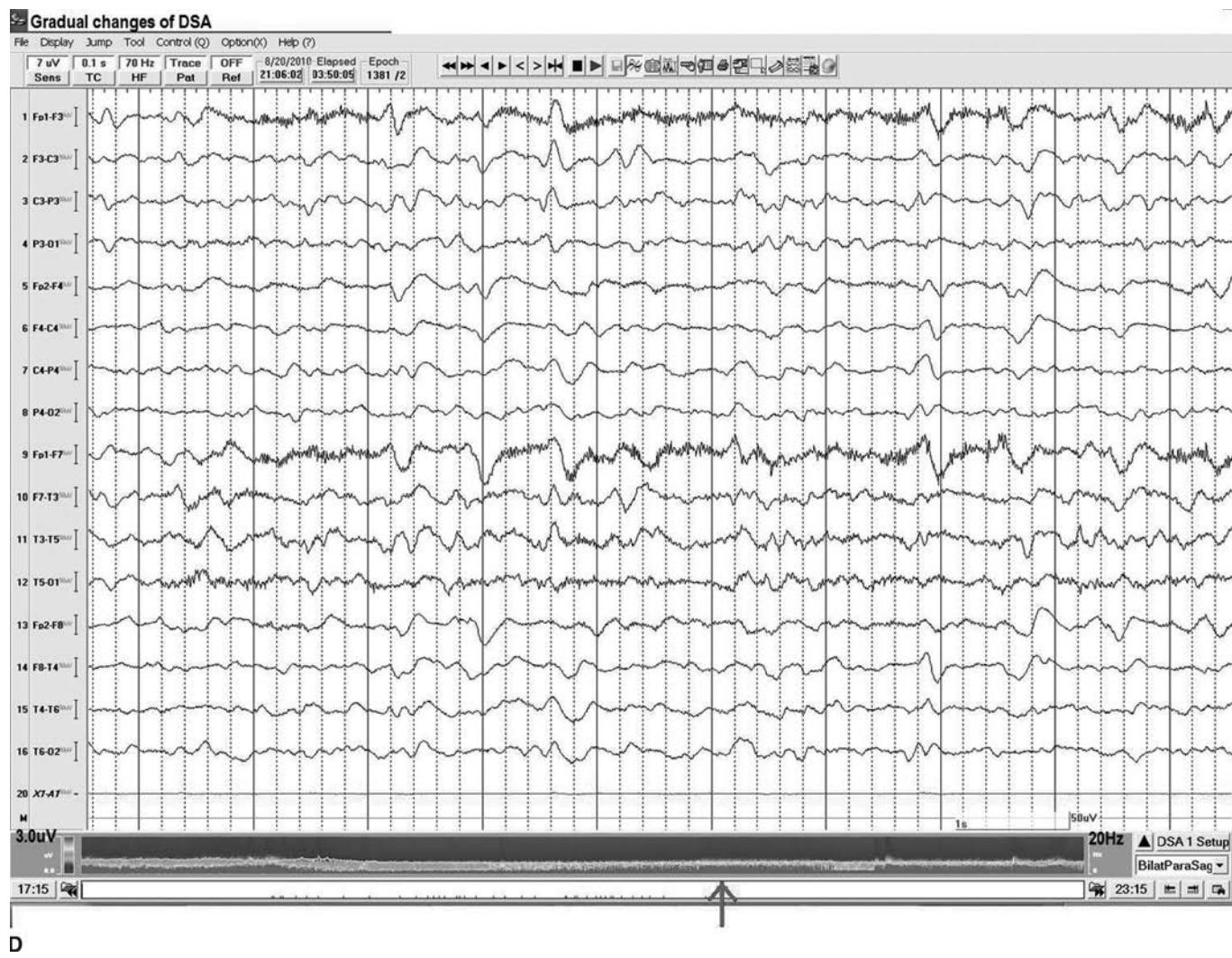
**Figure 10-6.** This is 6 hours DSA showing the episodes of gradually changing spectral power. At the time of low power (indicated by arrow in A), EEG showed diffuse delta and interspersed 5 to 6 Hz theta activities. The gradual increase of DSA power corresponded to a subtle increase of delta and theta activities (B,C; indicated by arrow), and at the time of maximum power, there were some appearances of triphasic waves (D). These gradual changes were difficult to be recognized by page-by-page mode of EEG review even by a seasoned electroencephalographer, but DSA profile clearly assisted to confirm the changes. (See color insert.)

**B****Figure 10-6. Cont'd.** (See color insert.)



C

**Figure 10-6. Cont'd.** (See color insert.)



**Figure 10-6. Cont'd.** (See color insert.)

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## SECTION IV

# Sleep Studies

CHAPTER

11

Mark Eric Dyken  
Adel K. Afifi  
Kyoung Bin Im

## Sleep Physiology and Pathology

**Note from the editor:** Material in this chapter is more in depth and more difficult than is necessary for a beginning Polysomnography Technologist. It is included here for the benefit of Neurology residents and fellows. It may well benefit the technologist who is searching for an advanced level of practice once a more basic understanding and knowledge has been mastered.

### INTRODUCTION

The knowledgeable and effective assessment and treatment of many sleep-related pathologies in neurological disease demands a basic understanding of the normal anatomy and physiology of the central nervous system (CNS) wake, sleep, and respiratory mechanisms. This approach can be utilized through a review of some major sleep disorders associated with neurological comitants described in the International Classification of Sleep Disorders (ICSD), which include narcolepsy with cataplexy (which may be the result of a genetic predisposition to CNS autoimmune disease) and obstructive sleep apnea (OSA) (where traditional thinking suggests a cause-and-effect relationship between stroke and OSA when brainstem areas of respiratory control are affected). The signs and symptoms associated with these disorders aid in localizing dysfunction to variable areas in the brainstem, hypothalamus, thalamus, and cortex, thus often directing confirmatory electrophysiological studies, and subsequent therapeutic interventions that are frequently directed toward correcting suspected associated deficiencies in monoaminergic, cholinergic, and orexin/hypocretin neurotransmitter systems.

### BASIC CNS ANATOMY AND PHYSIOLOGY OF SLEEP

#### HISTORICAL PERSPECTIVE

Constantin Freiherr von Economo's studies of the viral encephalitis lethargica (von Economo's disease) (that resulted from a pandemic, which occurred from approximately 1915 to 1924) indicated the existence of specific wake and sleep centers in the brain residing in the posterior and anterior hypothalamus, respectively.<sup>1,2</sup> This was complemented by Bremer's isole preparations in the 1920s and the early studies of Moruzzi and Magoun in the 1940s, which helped identify the ascending reticular formation (a brainstem reticular core mass of neurons and nerve fibers extending from the caudal medulla to the rostral mesencephalon) that connected the various specific wake and sleep centers and supported normal patterns of sleep and wakefulness.<sup>3-5</sup>

#### WAKEFULNESS MECHANISMS

The ascending reticular activating system utilizes monoaminergic and cholinergic neurotransmitter systems to promote wakefulness.<sup>5</sup> The monoaminergic component includes the hypothalamic tuberomammillary nucleus (TMN) and the norenergic locus coeruleus (LC) of the brainstem. The cholinergic system functions through the brainstem pedunculopontine/lateral dorsal tegmental nuclear (PPN/LDTN) complex, and comprises "REM sleep-off" and "REM sleep-on" cells, which are most active during wakefulness and rapid eye movement (REM) sleep, respectively.<sup>6</sup>

Wakefulness is promoted by the PPN/LDTN through two pathways that eventually lead to diffuse cortical projections; a ventral hypothalamic route [which stimulates the TMN and the orexin/hypocretin neurons located in the lateral nucleus (LN) of the hypothalamus] and a dorsal thalamic system (which excites nonspecific midline and intralaminar nuclei while inhibiting the reticular nucleus of the thalamus) (Fig. 11-1).<sup>6</sup>

### SLEEP-ONSET MECHANISMS

Sleep onset is promoted largely by a hypothalamic “sleep switch” located in the preoptic area of the hypothalamus (the ventrolateral and median preoptic nuclei), which has reciprocal inhibitory connections with the previously mentioned waking centers (Fig. 11-2).<sup>7,8</sup> Gradual inhibition of “REM sleep-off” cells in the PPN/LDTN leads to disinhibition of the reticular nucleus of the thalamus, thus allowing cortical generation of non-rapid eye movement (NREM) sleep through limbic forebrain connections.<sup>9</sup>

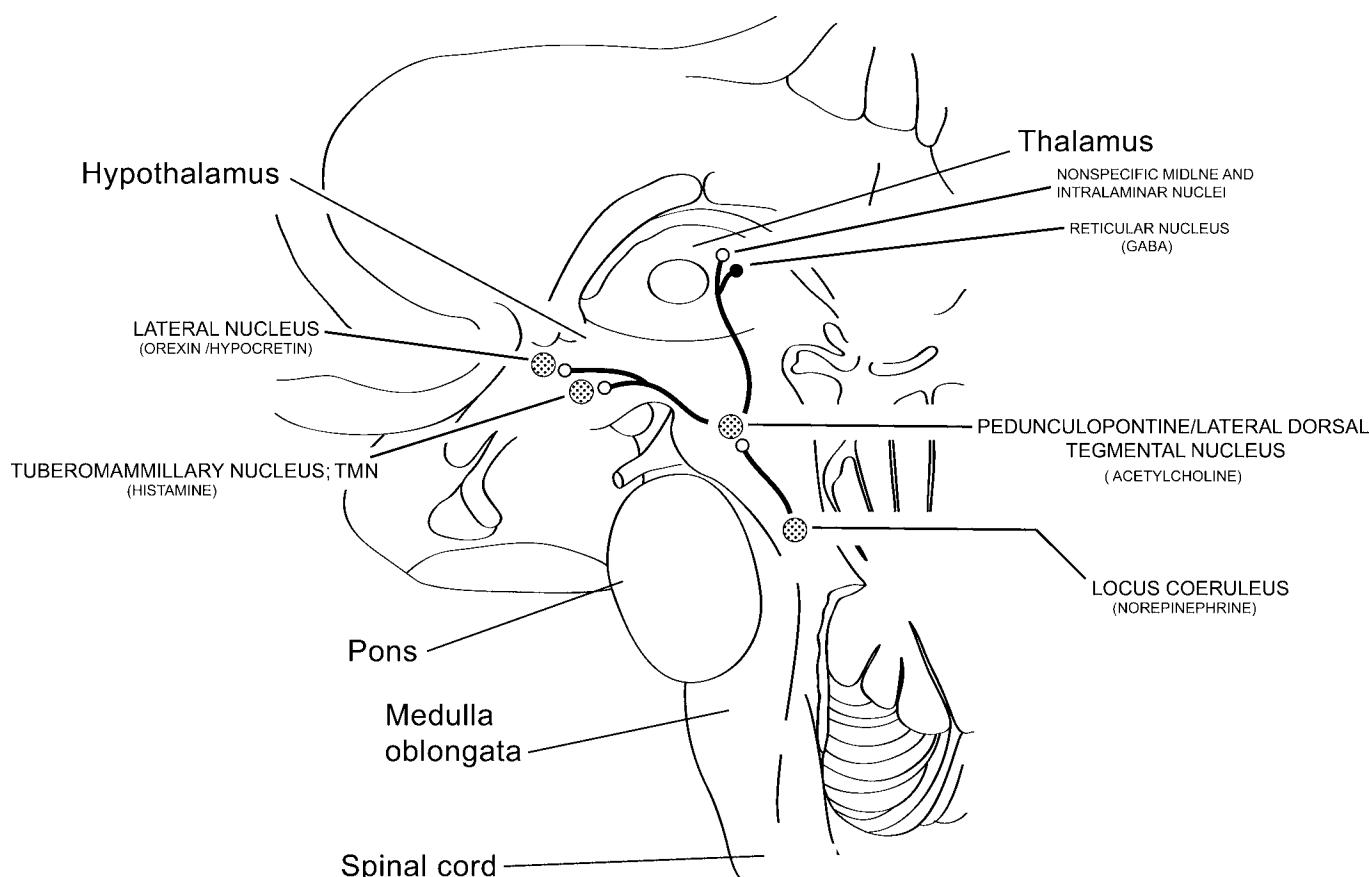
## SLEEP PATHOLOGY

In this section, disturbances of sleep mechanism are discussed by referring to two major sleep disorders: narcolepsy and sleep apnea in relationship to stroke.

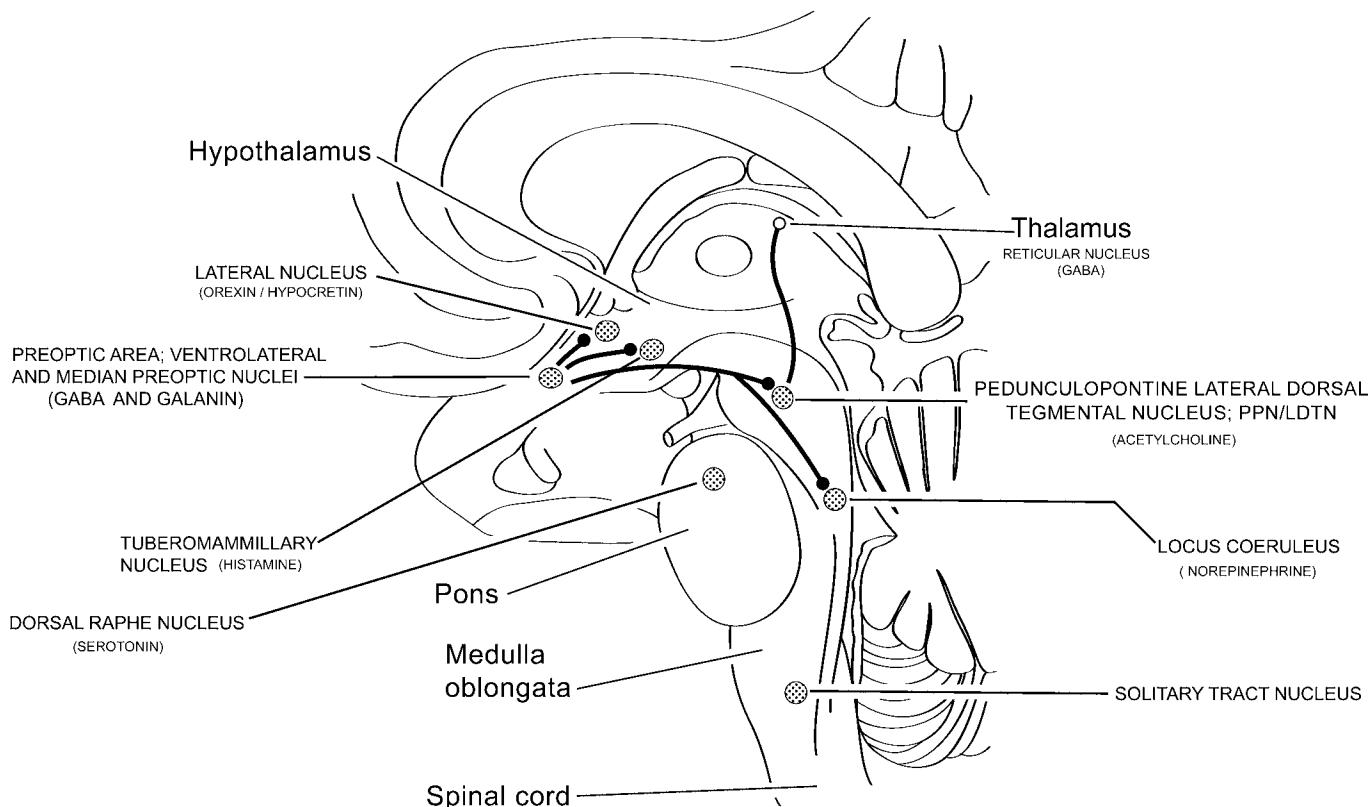
### REM SLEEP MECHANISMS APPRECIATED THROUGH NARCOLEPSY WITH CATAPLEXY

#### Clinical

Narcolepsy with cataplexy is most appropriately characterized in the ICSD as a “Hypersomnia of Central Origin,” as it is due to a dysfunction of central REM sleep mechanisms clinically evidenced as sleep attacks, cataplexy (weakness precipitated by strong emotions, usually laughter), hypnagogic (at sleep onset) and hypnopompic (upon awakening) hallucinations, and sleep paralysis.<sup>10</sup>



**Figure 11-1.** Basic wake systems. Diagrammatic representation of the brainstem in the parasagittal plane showing the mechanism and structures involved in the generation of wakefulness. Cholinergic cells in the PPN/LDTN complex have two waking pathways, leading to diffuse cortical projections. A ventral hypothalamic system excites the tuberomammillary and the orexin/hypocretin neurons in the perifornical lateral nucleus of the hypothalamus, which relay to cholinergic basal forebrain cells, while a dorsal thalamic route stimulates nonspecific midline and intralaminar nuclei (while inhibiting the reticular nucleus of the thalamus). (Open circle, facilitatory; closed circle, inhibitory.) (Modified from Dyken ME, Yamada T. Narcolepsy and disorders of excessive somnolence. In: Ballard RD, Lee-Chiong TL Jr, eds. *Primary Care: Clinics in Office Practice*. Elsevier Saunders, 2005:389–413; Fig. 1, with permission.)



**Figure 11-2.** Basic sleep-onset systems. Diagrammatic representation of the brainstem in the parasagittal plane showing the proposed mechanism and structures involved in sleep onset. Excited nuclei in the preoptic area of the hypothalamus (the ventrolateral and median preoptic nuclei) use inhibitory neurotransmitters [gamma-aminobutyric acid (GABA) and galanin] in reciprocal inhibitory relays with waking centers, and in direct thalamic projections. Gradual inhibition of “REM sleep-off” cells, which function through the PPN/LDTN, leads to disinhibition of GABAergic reticular thalamic nuclei that generate NREM sleep through intrathalamic connections to limbic forebrain structures that include the orbitofrontal cortex. Sleep is also facilitated by the solitary tract nucleus, utilizing unknown neurotransmitters, through direct connections with the hypothalamus, amygdala, and other forebrain structures. Serotonergic neurons in the midline (raphe) of the medulla, pons, and mesencephalon of the brainstem help modulate sleep. (Open circle, facilitatory; closed circle, inhibitory.) (Modified from Dyken ME, Yamada T. Narcolepsy and disorders of excessive somnolence. In: Ballard RD, Lee-Chiong TL Jr, eds. *Primary Care: Clinics in Office Practice*. Elsevier Saunders, 2005:389–413; Fig. 1, with permission.)

### REM Sleep Mechanisms

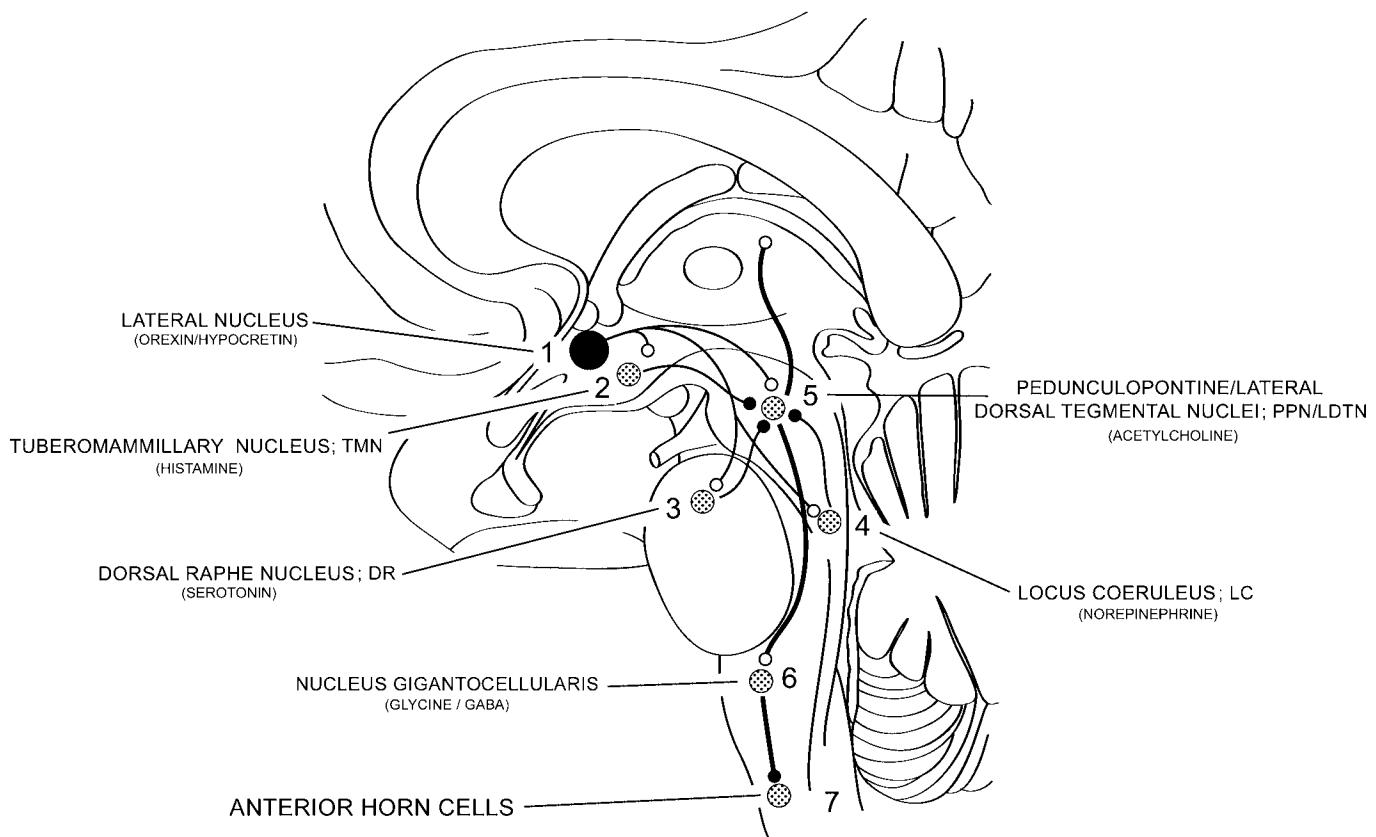
The symptoms of narcolepsy result from a paucity of wake-promoting neuropeptides (orexins/hypocretins) in the LN of the hypothalamus, which leads to cerebrospinal fluid levels of hypocretin-1  $\leq 110$  pg/mL in more than 90% of narcoleptics with cataplexy, and a loss of wake-promotion on the PPN/LDTN, TMN, brainstem dorsal raphe (DR) nucleus, and LC (Fig. 11-3).<sup>10–12</sup> Subsequently, the inactivated DR (serotonergic) and LC nuclei allow disinhibition of “REM sleep-on” cells that function through the PPN/LDTN.<sup>13</sup> The disinhibited “REM sleep-on” cells project rostrally to several thalamic nuclei producing, through diffuse cortical connections, a REM sleep electroencephalogram (EEG) pattern, and caudally to the medullary nucleus gigantocellularis producing REM atonia/weakness through the inhibition of alpha motor neurons.<sup>14,15</sup> Symptoms of narcolepsy have also been associated with hypothalamic dysfunction and reduced orexin/hypocretin CSF levels in a variety of other neurologic conditions including CNS infections, head trauma, brain tumors, multiple sclerosis, and dementia.<sup>10</sup>

In normal REM, or otherwise often referred to as *dreaming sleep*, the medially situated nucleus reticularis pontis caudalis appears to be the generator site of pontine-geniculo-occipital (PGO) spikes, whose throughput to the forebrain is via the

PPN/LDTN. McCarley and Hobson correlated REM physiology with dreaming utilizing the phenomena of PGO spikes. A variety of physiologically phasic activity, including REMs, and vestibular, motor, and middle-ear-muscle activity, has been associated with PGO spikes. During active REM, the PGO spikes in a sense organize and present this varied phasic activity to the entire brain through a corollary discharge system, which then allows an individual to recognize the activity as normal dream. In a patient with narcolepsy, this activity could potentially be appreciated as a hypnagogic/hypnopompic hallucination.<sup>16–18</sup>

### Polysomnography

On polysomnogram (PSG) analysis, REM sleep is associated with a “relatively low voltage, mixed frequency EEG” with alpha (8–13 Hz) and theta (4–7 Hz) waveforms and “saw-tooth” (2–6 Hz) central waves, an electrooculogram with REMs, and an atonic electromyogram (EMG) (Fig. 11-4; see also Fig. 13-1).<sup>19</sup> In narcolepsy with cataplexy, a modified PSG, called the *multiple sleep latency test*, reveals sleep-onset REM periods, while video-PSG studies during REM-related symptoms have shown REM sleep patterns in awake patients who can respond appropriately during a clinical examination (Fig. 11-5).<sup>10,20</sup>



**Figure 11-3.** The brain and the brainstem in the parasagittal plane showing the basic proposed mechanism and structures involved in generation of REM-sleep phenomena in narcolepsy. The paucity of orexin (hypocretin) cells in the lesioned lateral nucleus of the hypothalamus (1) results in a loss of wake-promoting effects on the tuberomammillary nucleus (2), the dorsal pontine raphe nucleus (3), the locus coeruleus (4), and the pedunculopontine/lateral dorsal tegmental nucleus (PPN/LDTN) (5). This leaves cholinergic “REM-sleep on” related cells in the PPN/LDTN (5) uninhibited, allowing stimulation of the nucleus gigantocellularis (6), which then hyperpolarizes anterior horn cells (7) in the spinal cord, resulting in atonia. (Open circle, facilitatory; closed circle, inhibitory; large closed circle, lesioned lateral nucleus of the hypothalamus.) (Modified from Dyken ME, Yamada T. Narcolepsy and disorders of excessive somnolence. In: Ballard RD, Lee-Chiong TL Jr, eds. *Primary Care: Clinics in Office Practice*. Elsevier Saunders, 2005:389–413; Fig.1, with permission.)

### Therapy

Amphetamines have a chemical structure similar to the endogenous catecholamines norepinephrine (NE) and dopamine (DA), and they were among the first effective drugs used to treat narcolepsy (Fig. 11-6).<sup>21</sup> Amphetamines override narcoleptic hypothalamic deficits through catecholaminergic effects on brainstem wakefulness centers; the noradrenergic LC, and the dopaminergic mesencephalic ventral tegmental area of Tsai and medial substantia nigra.<sup>22,23</sup> Amphetamines inhibit uptake and enhance release of DA and NE.<sup>22,23</sup> During narcoleptic REM-related symptoms, inactivation of the noradrenergic LC allows disinhibition of the cholinergic “REM sleep-on” cells of the PPN/LDTN, whereas the adrenergic effects of amphetamines inhibit “REM sleep-on” cells.<sup>22–24</sup>

In experimental animals with narcolepsy, central and systemic administration of orexin/hypocretin can prevent cataplexy.<sup>25</sup> In addition, sustained viability of the cells that produce this protein has been demonstrated in transplants from newborn rats to adult animals.<sup>26</sup>

Genetic markers for narcolepsy exist on the major histocompatibility complex of chromosome 6, and mapping of specific human leukocyte class II antigens (DR2 and DQ1) reveals a subtype human leukocyte antigen allele DQB1\*0602 in over

90% of narcoleptics with cataplexy.<sup>27</sup> This suggests a genetic predisposition to autoimmune disease, where abnormal coding of orexin/hypocretin cells might predispose them to virally inducible changes, leaving the LN of the hypothalamus prone to autoimmune injury.<sup>28</sup> As such, therapeutic regimens could conceivably include routine genetic screening and immunization of high-risk patients.

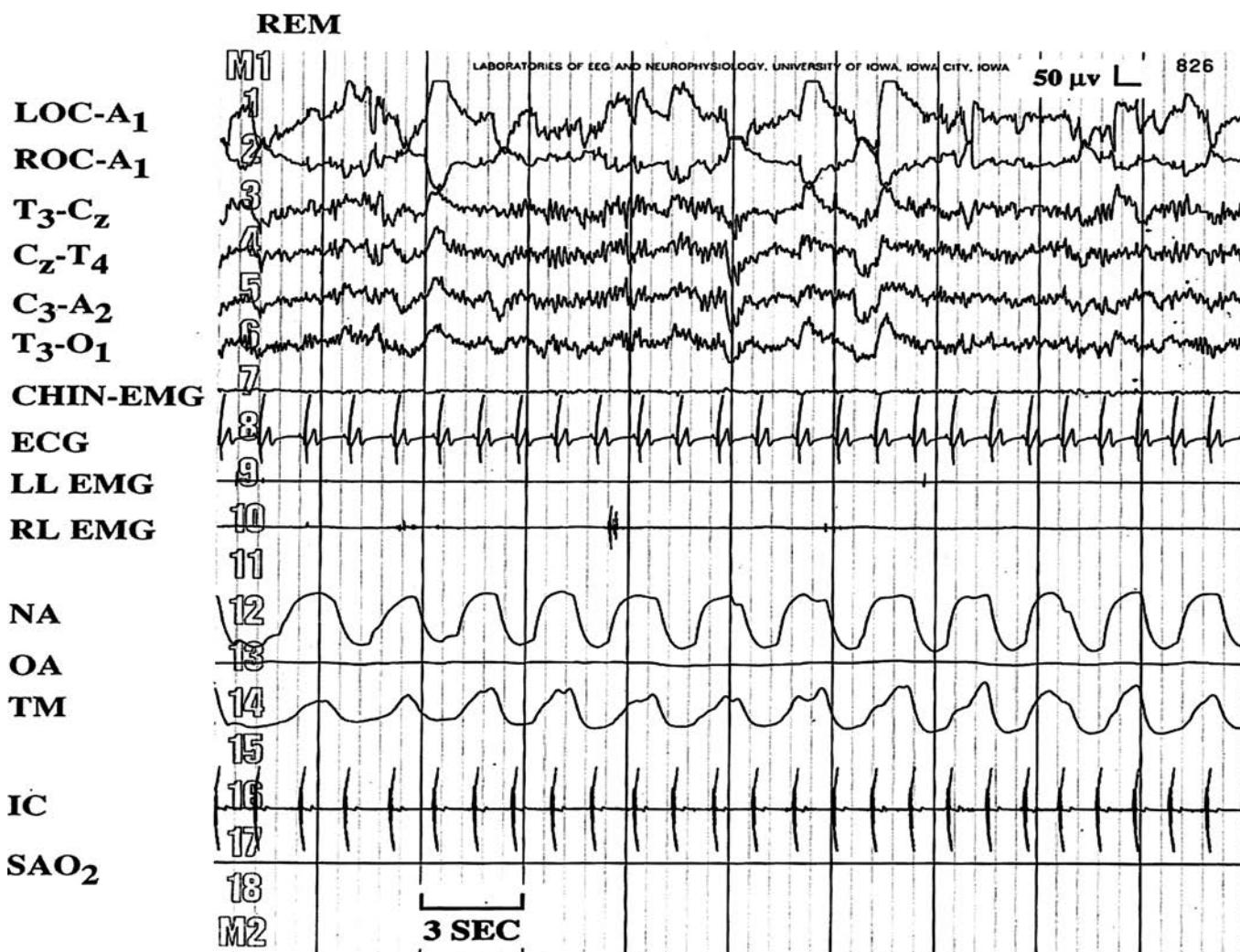
### OBSTRUCTIVE SLEEP APNEA AND STROKE

#### Background

Case-control and cross-sectional studies have shown a strong association between OSA and stroke.<sup>29,30</sup> Although traditional thinking suggests stroke can cause apnea, cohort studies indicate OSA is a stroke risk factor.<sup>30</sup> Nevertheless, no double-blinded randomized controlled, treatment versus nontreatment clinical trials utilizing PSG provide strong scientific evidence that OSA can routinely lead to stroke.

#### The Association Between OSA and Stroke

In 1991, our observation of an obese man with a history of snoring and sleepiness, diagnosed with OSA after awakening with a



**Figure 11-4.** The PSG of normal REM sleep in a young adult reveals a marked reduction of EMG activity with occasional bursts of muscle activity associated with rapid eye movements. The background EEG activity shows relatively low-voltage, mixed-frequency activity with slow alpha/theta patterns and intermittent 3-Hz “sawtooth” patterns in the frontal and the vertex regions. (LOC, left outer canthus; ROC, right outer canthus; A<sub>1</sub>, left ear; T, temporal; C, central; O, occipital; EMG, electromyogram; ECG, electrocardiogram; LL, left leg; RL, right leg; NA, nasal airflow; OA, oral airflow; TM, thoracic movement; IC, intercostal EMG; SAO<sub>2</sub>, oxygen saturation.) (From Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Semin Neurol* 2001;21:377–390; Fig. 5, with permission.)

hemorrhagic stroke suggesting a sleep-related hypertensive event, led to a case-control study that proved an association between OSA and stroke.<sup>31</sup> In 1992, using PSG, we studied 24 consecutively encountered inpatients with acute stroke, and 27 healthy gender- and age-matched control subjects without stroke.<sup>29,32</sup> Significant OSA was found in 71% of stroke subjects, and in only 19% of controls.

#### CNS Injury as a Risk for OSA

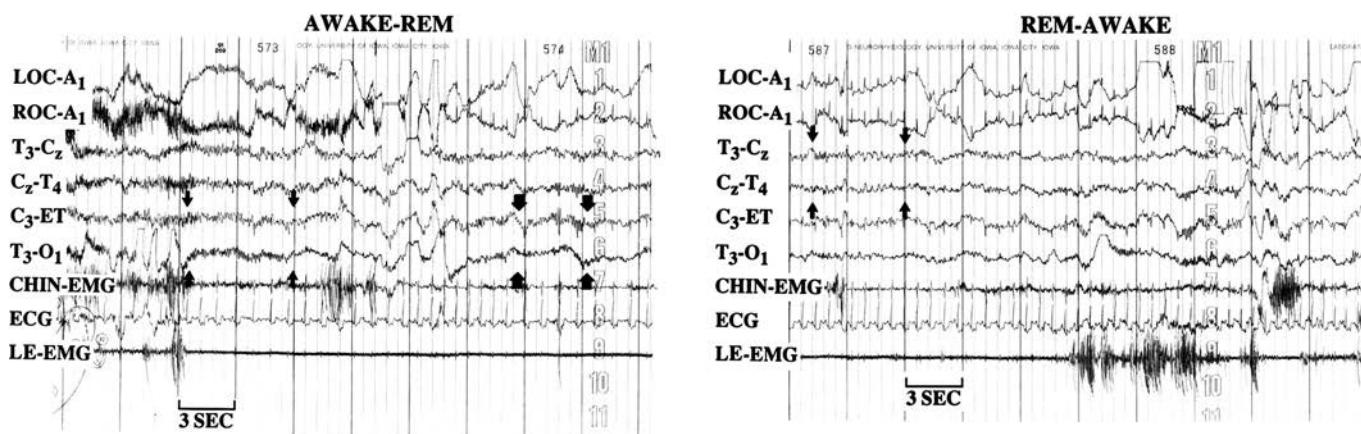
Animal experiments and human studies suggest brainstem stroke can cause apnea if one of two areas for automatic respiration in the medulla oblongata is affected: the dorsally situated nucleus solitarius, and the more ventrolaterally located nucleus ambiguus.<sup>33–35</sup> Central apnea can occur after injury to the nucleus solitarius due to diaphragmatic dysfunction, while damage to

upper airway motor neurons in the nucleus ambiguus can lead to OSA (Figs. 11-7 and 11-8).<sup>36,37</sup>

Our study of a 32-year-old man with viral encephalitis emphasizes the fact that diffuse CNS injury affecting diencephalic and cortical areas of respiratory control can also lead to apnea.<sup>38–40</sup> While ill, our patient's PSG revealed OSA with an apnea/hypopnea index [(AHI), the average number of obstructive events per hour of sleep] of 25.4 (Fig. 11-9). Immediately after his encephalopathy resolved, a repeat PSG showed complete resolution of OSA, including during REM sleep in the supine position.

#### OSA as a Risk for Stroke

Arzt et al.'s<sup>30</sup> study of a stratified random sample from the Wisconsin Sleep Cohort Study proved OSA to be a stroke risk factor. These investigators determined the incidence of stroke



**Figure 11-5.** Immediately after being told a joke, a patient with narcolepsy developed sudden quadripareisis. **Left**, polysomnography revealed a marked reduction of electromyographic activity with occasional bursts of muscle activity that occurred in strong association with rapid eye movements. Concomitantly, the EEG revealed the sudden loss of normal waking 8- to 13 Hz activity (outlined by the four *small arrows*) with replacement by the typical slow alpha/theta patterns of REM sleep (outlined by the four *large arrows*). **Right**, during polysomnographic REM, the patient intermittently exhibited classic, 3-Hz sawtooth electroencephalographic patterns in the vertex regions (outlined by the four *arrows*). After conversing in a coherent manner for approximately 7 minutes, he suddenly regained the capacity for movement and the EEG simultaneously returned to a normal awake pattern. (LOC, left outer canthus; ROC, right outer canthus; ET, ears tied; LE, lower extremity.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC, et al. Diagnosing narcolepsy through the simultaneous clinical and electrophysiologic analysis of cataplexy. *Arch Neurol* 1996;53:459-460; Fig. 1, with permission.)

at 4-year intervals over a 12-year period. After controlling for age and gender, subjects with a baseline AHI  $\geq 20$  had a significantly higher odds ratio for the incidence of stroke compared to individuals without OSA.

#### Possible Mechanisms for Apnea-Induced Stroke

**THE METABOLIC SYNDROME.** OSA increases the odds of having the metabolic syndrome by nine. OSA is also independently associated with obesity and hypertension (stroke risk factors that are included in the metabolic syndrome).<sup>41</sup> An increase in body mass index (weight in kilograms divided by the square of the height in meters) by 1-standard deviation has been reported to increase the odds ratio for sleep-disordered breathing (defined as an AHI  $\geq 5$ ) by 4.17.<sup>42</sup> In addition, a prospective, population-based study showed that over a 4-year period, the odds of an individual with an AHI either between 5.0 and 14.9 or  $\geq 15.0$  for developing hypertension were two and three times, respectively, greater than for someone without significant apnea.<sup>43</sup>

**AUTONOMIC ACTIVITY.** OSA elevates sympathetic nerve activity (SNA) as a result of the reflex effects of hypoxia, hypercapnia, and decreased input from thoracic stretch receptors.<sup>44</sup> Our hypothesis that OSA-induced hypertension could cause stroke was supported by microneurographic studies that directly measured efferent SNA from postganglionic unmyelinated C-fibers.<sup>45,46</sup> In ten subjects with OSA, we showed an increase in SNA by 246% during the last 10 seconds of apnea, in association with a mean blood pressure increase from 92 mm Hg in the waking state to 127 mm Hg in REM sleep (Figs. 11-10 and 11-11).<sup>47</sup> In addition, documentation of persistently elevated waking sympathetic tone suggested OSA could induce chronic changes that predispose to stroke.<sup>46,47</sup>

Autonomic effects may also explain the high prevalence of cardiac arrhythmias reported in up to 48% of apneics (Fig. 11-12).<sup>48,49</sup> We have shown obstructive apneas can also

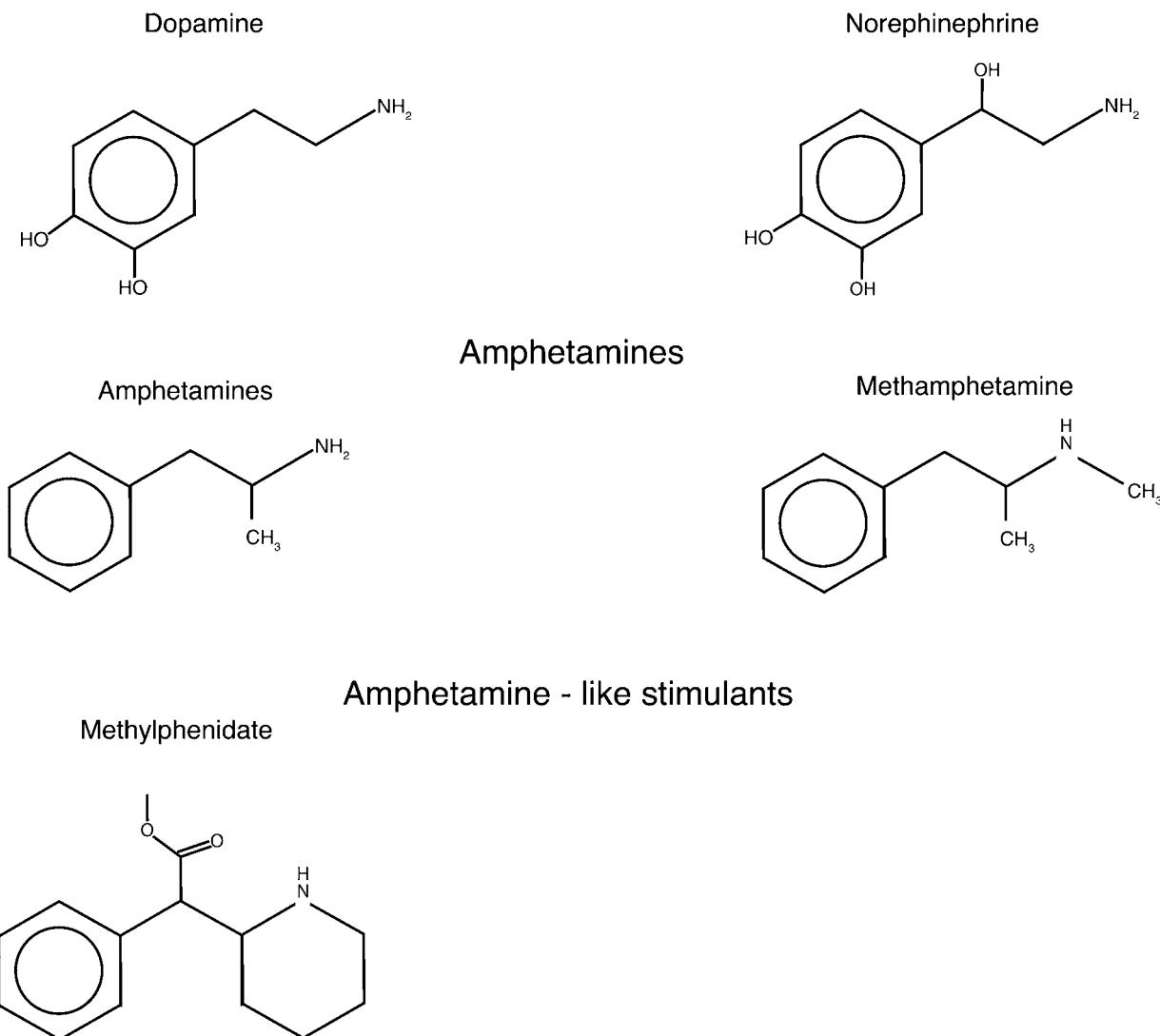
lead to excessive parasympathetic responses associated with inspiring against a closed glottis (a relative "Mueller maneuver").<sup>50,51</sup> This was evidenced in one study as recurrent prolonged episodes of sinus arrest and dramatic reductions in blood pressure from 180/100mmHg (prior to obstructions) to systolic pressures <50mmHg during obstructions.<sup>52</sup> In patients with atrial fibrillation (AF), the risk of OSA has been reported to be 49%, and noncompliance with continuous positive airway pressure (CPAP) has been associated with a greater recurrence rate of AF after cardioversion.<sup>53,54</sup> AF is a strong risk factor for stroke, and it may also contribute to stroke in some patients with OSA.

**CIRCADIAN RHYTHMS.** If stroke has an equal probability of occurring at any time during a 24-hour time frame, 33% should occur during an 8-hour period of sleep. Nevertheless, ischemic stroke has been reported to occur with a relatively high frequency during sleep and in the early morning hours.<sup>55</sup> This is complemented by our study of apnea in acute stroke, where we found a higher-than-expected percentage of subjects with OSA experiencing their strokes during sleep (54%;  $p = 0.0304$ ).<sup>32</sup>

**REM PARESIS.** The most prolonged period of REM sleep occurs during the early morning hours, coinciding with the greatest circadian risk for stroke. The paresis of REM sleep generally worsens OSA and may potentiate the risk for stroke during this longer time frame.

**PHYSIOLOGICAL SYMPATHETIC NERVOUS SYSTEM ACTIVATION.** REM sleep is normally a state of significantly elevated SNA with blood pressures that reach normal waking levels, and pressure surges that occur in association with REM-related muscle twitches (phasic REM periods).<sup>56</sup> A negative amplification of these autonomic phenomena has been documented in OSA.

## Endogenous Catecholamines



**Figure 11-6.** Comparison of chemical structures of endogenous catecholamines with amphetamines and amphetamine-like stimulants. (Modified from Nishino S, Mignot E. Wake-promoting medications: basic mechanisms and pharmacology. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2005:468–483; Fig. 38-1, with permission.)

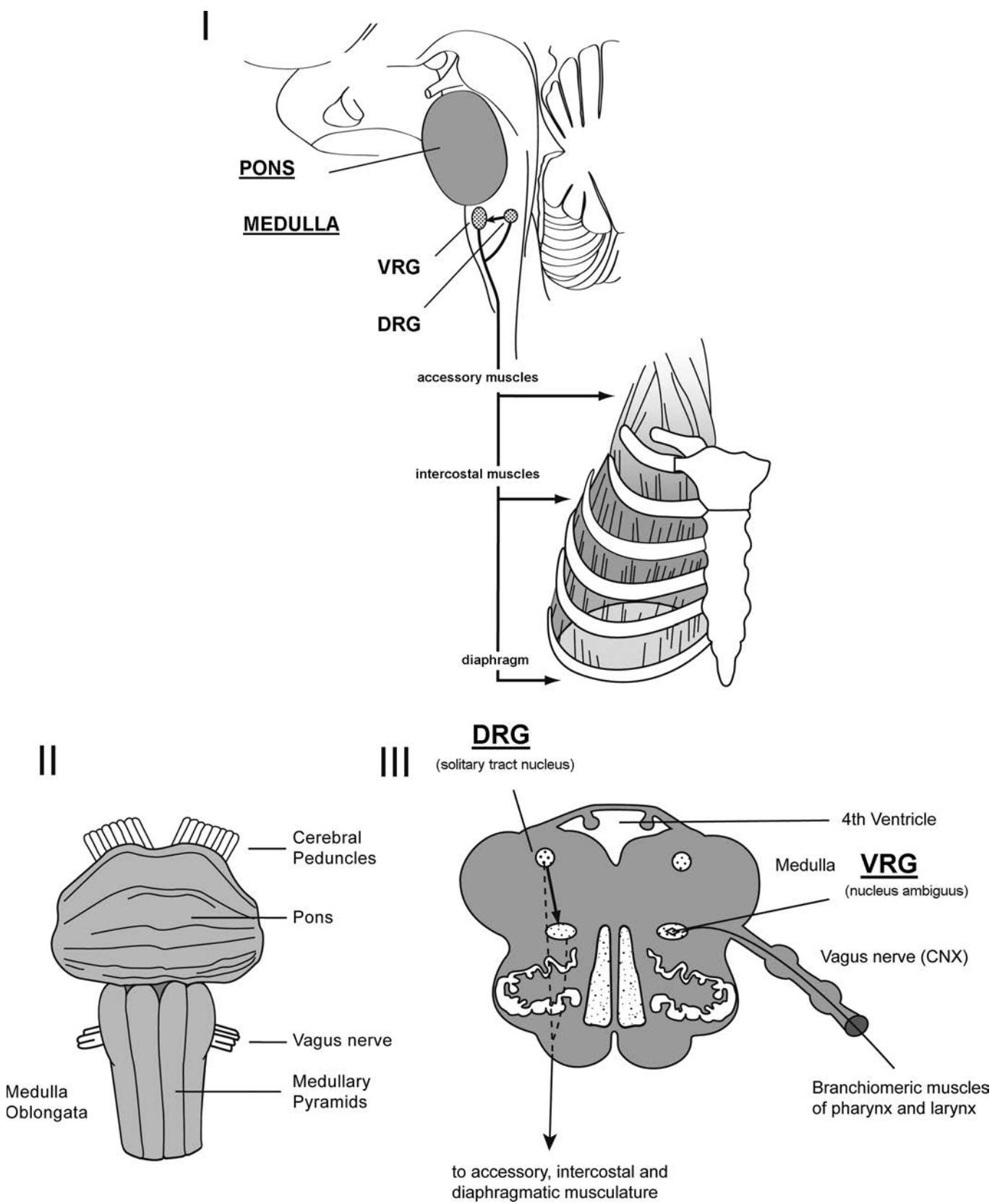
**CEREBRAL BLOOD FLOW.** Cerebral blood flow normally increases in REM sleep, whereas obstructive apneas can increase intracranial pressure and reduce cerebral perfusion pressure.<sup>57,58</sup> In OSA, these elements, when combined with a REM-related increase in SNS activity (and its concomitant blood pressure instability), might synergistically predispose to stroke.

**HEMATOLOGICAL.** The early morning hours are associated with low fibrinolytic activity and high levels of catecholamines, blood viscosity, and platelet activity and aggregability, at a time when REM-related SNA and hemodynamic instability might potentiate platelet aggregation and plaque development.<sup>59</sup> In this normal hematological milieu, the elevation of catecholamines and platelet activation associated with OSA may further increase thrombus and embolus formation, and stroke risk.<sup>60,61</sup>

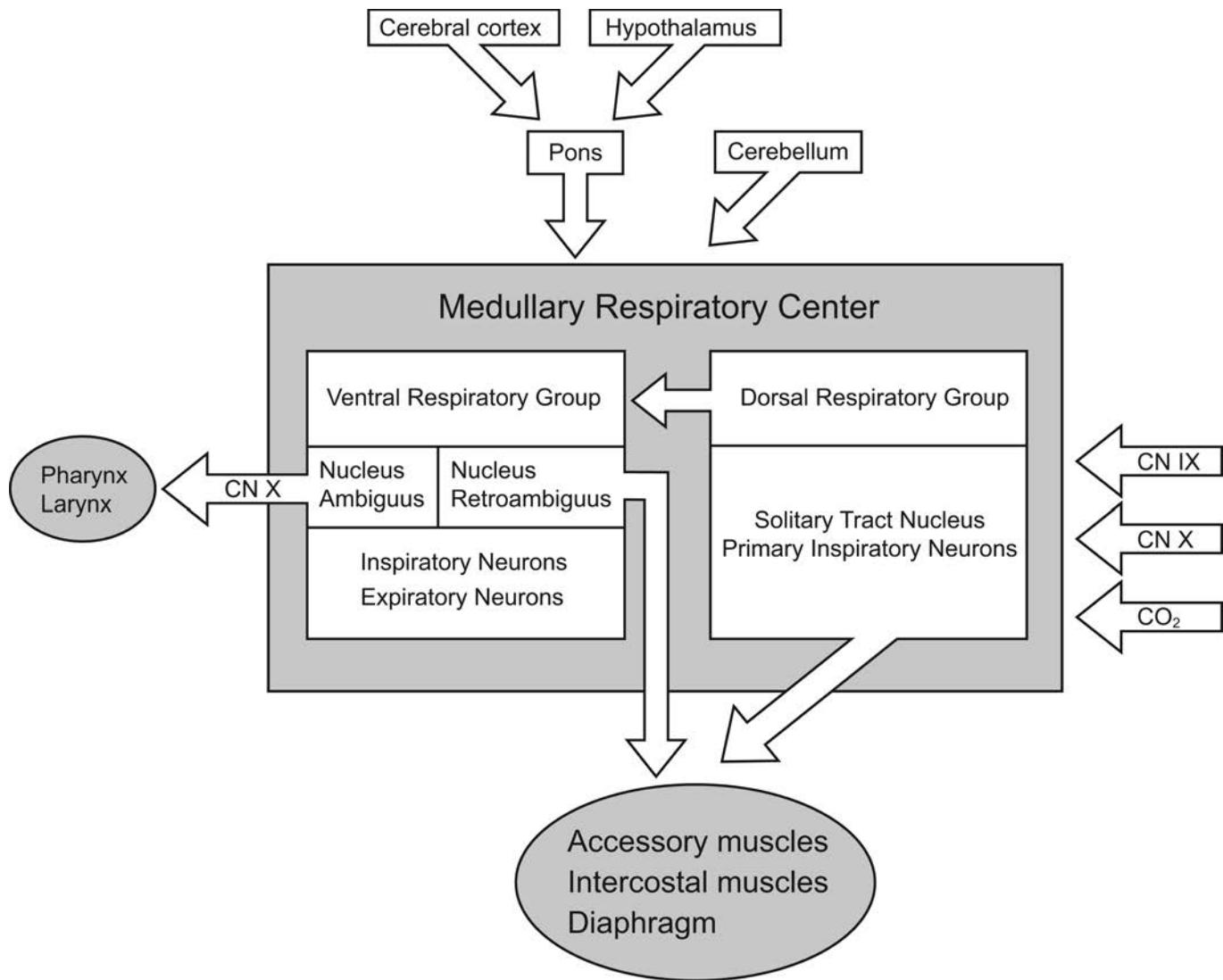
Increased levels of two proteins associated with platelet activation [soluble CD40 ligand (sCD40L) and soluble P-selectin (sP-selectin)] have been related to silent brain infarctions (SBIs).<sup>62</sup> Minoguchi et al. utilized brain MRIs to compare the prevalence of SBI in 50 men with OSA and 15 healthy controls. SBI was found in 25% of subjects with moderate-to-severe OSA and in 6.7% of controls. The serum levels of sCD40L and sP-selectin were significantly higher in the apneic group, and treatment with CPAP led to significant reductions of these levels.

### **Treatment Versus Nontreatment Studies**

In 1990, Partinen et al.<sup>63,64</sup> published the results of a 7-year study where 198 patients with OSA were treated with tracheostomy (71) or weight loss only (127). At follow-up, 1.2% of the tracheostomy group suffered new stroke, while only 2.8% died,



**Figure 11-7.** This schematic diagram of the brain stem shows the location of the dorsal and ventral respiratory groups and their projections to the respiratory muscles. (Modified from Dyken MD, Afifi AK, Im KB. Stroke in sleep. In: Chokroverty S, Sahota P, eds. *Acute and Emergent Events in Sleep Disorders*. Oxford University Press, 2011:328–348; Fig. 19-5, with permission.)



**Figure 11-8.** This schematic diagram details the components and connectivities of the medullary respiratory center. (Modified from Afifi AK, Bergman RA. Medulla oblongata. In: Afifi AK, Bergman RA, eds. *Functional Neuroanatomy; Text and Atlas*. 2nd ed. New York, NY: McGraw-Hill; 2005:92-94; Figs. 5-18 and 5-19, with permission.)

whereas 5.2% in the weight loss group experienced new stroke, and 17.3% died (11% from vascular causes). These results suggest that undertreated OSA may lead to higher morbidity and mortality from stroke.

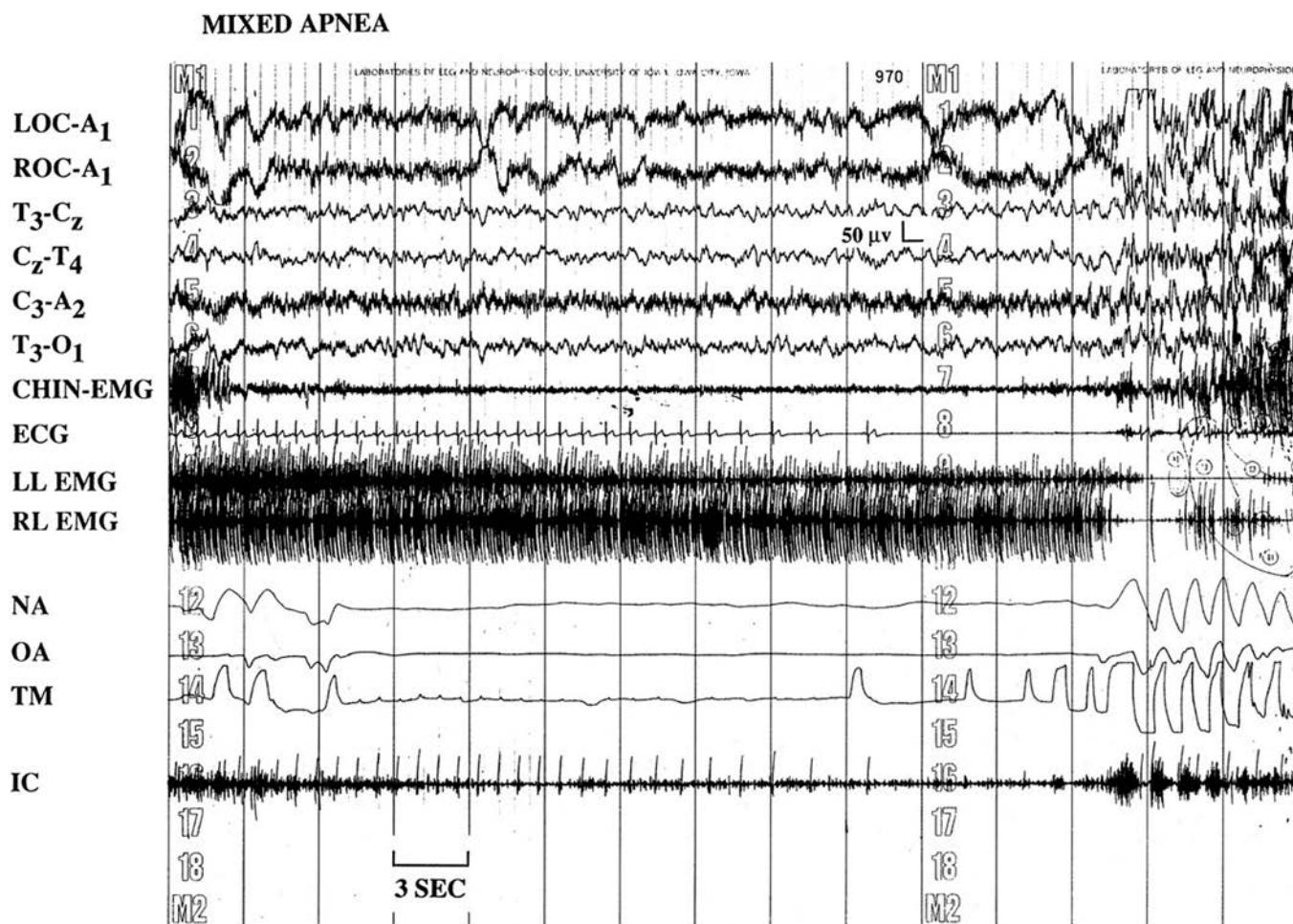
In a comparative, treatment versus nontreatment study, we showed OSA can lead to cerebral hypoxemia and death in critically ill patients.<sup>65</sup> Our treatment subject suffered a 90-second obstructive apnea with an oxygen saturation ( $\text{SaO}_2$ ) low of 31%, during which his EEG pattern became diffusely slow (suggesting hypoxemia) and was subsequently followed by an electrocerebral silence (ECS; flat/absent EEG activity) pattern (Fig. 11-13). He became cyanotic and required rescue breathing. After apparent full arousal, it took 45 seconds for his EEG to return to a normal waking pattern.

Our other patient could not receive CPAP or bilevel PAP therapy due to a do-not-resuscitate/do-not-intubate directive, where no heroic measure to sustain life was permissible. A 30-second obstructive apnea, associated with an  $\text{SaO}_2$  desaturation of 12%, led to a slow-wave EEG pattern that was followed

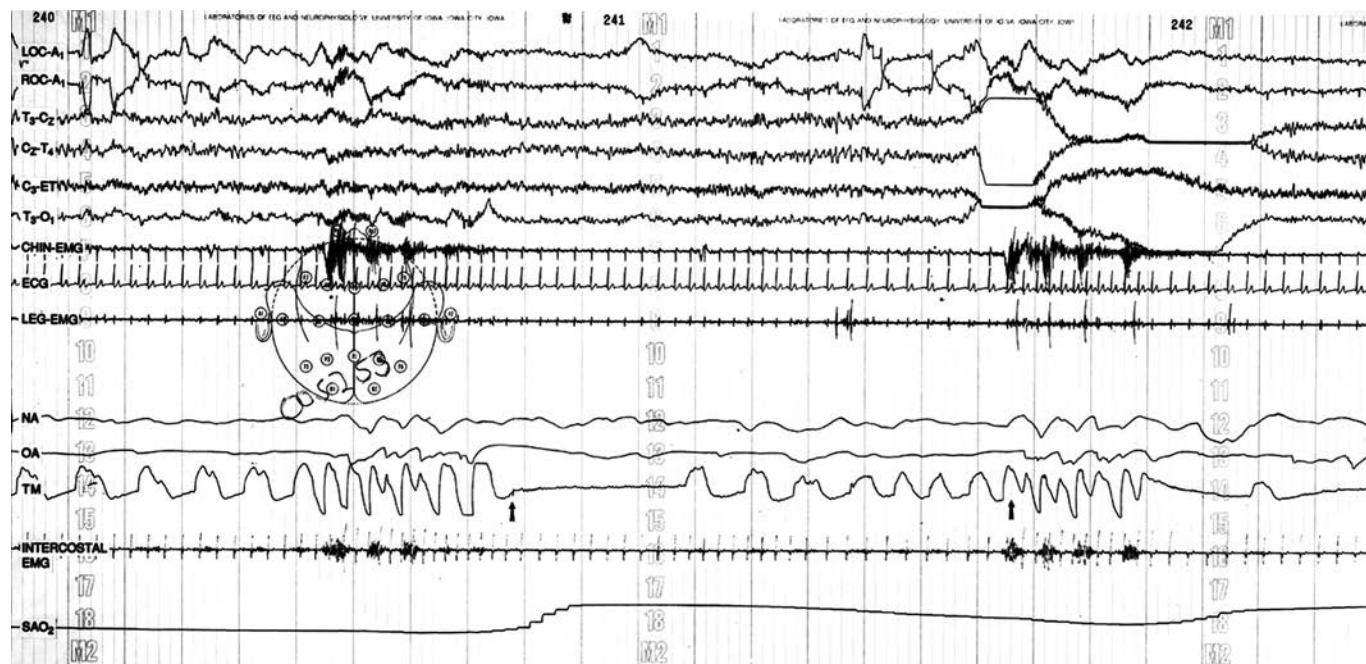
by ECS and a simultaneous heart rate reduction from 148 to 40 beats per minute (Figs. 11-14 and 11-15). Following this event, a series of central apneas was eventually followed by complete respiratory and cardiac arrest (Fig. 11-15).

#### **Poststroke Treatment of OSA: Morbidity and Mortality**

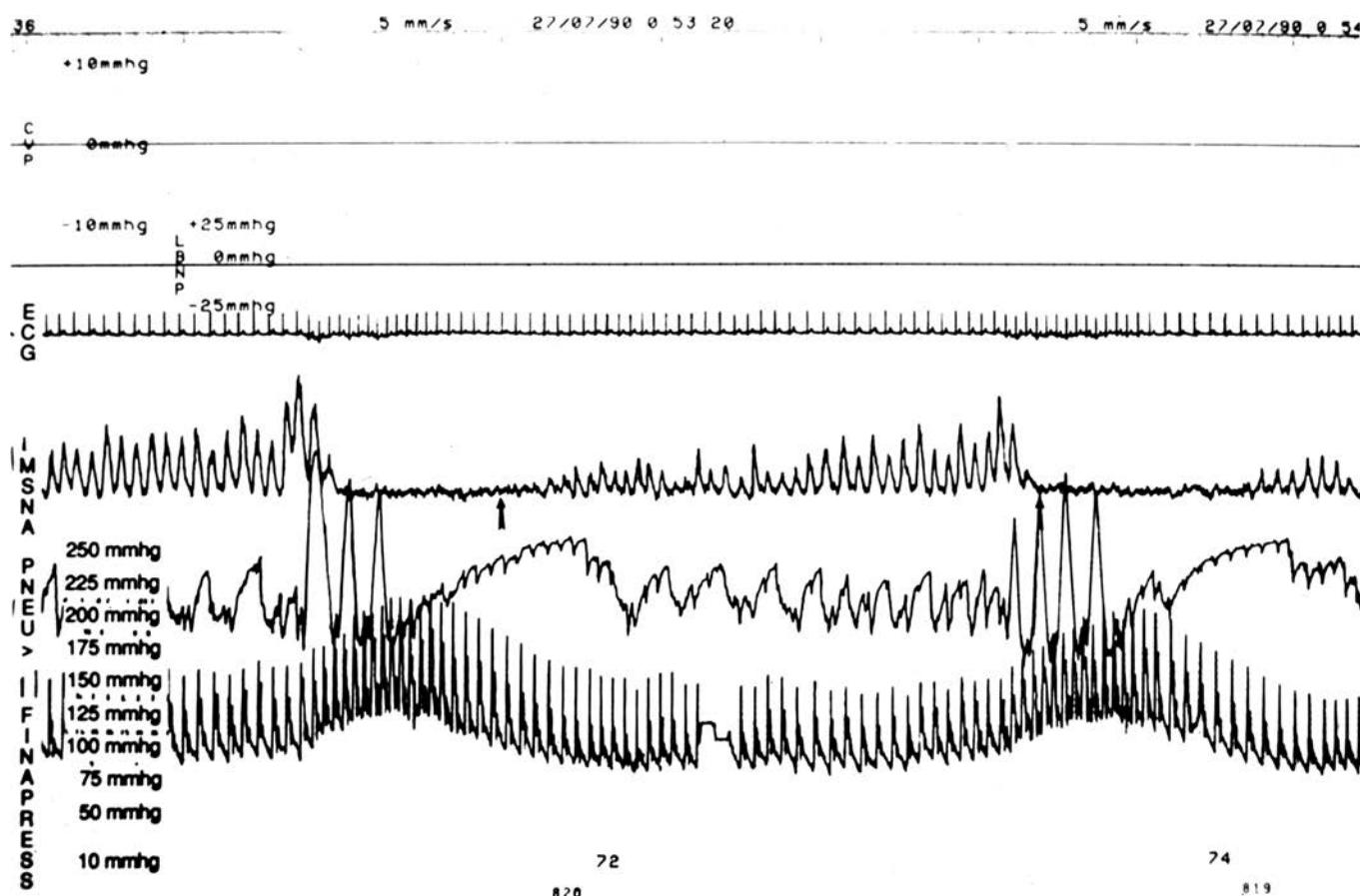
After stroke, the presence of OSA appears to increase morbidity and mortality. Good et al.<sup>66</sup> determined the functional abilities for 19 patients with recent stroke, of whom 95% were diagnosed with OSA. Hemispheric stroke with snoring and abnormal oximetry readings were predictive of worse functional outcome. Determining the effects of CPAP therapy on mortality and morbidity in stroke patients with OSA has been limited by long-term treatment compliance reported as low as 15%.<sup>67</sup> Brown et al.<sup>68</sup> suggest that if future clinical trials can prove treatment of OSA after stroke significantly improves morbidity and mortality, then routine screening for OSA in the stroke population might become a future consideration.



**Figure 11-9.** A previously healthy, 32-year patient with viral encephalitis and delirium alternating with stupor suffered the apparent new onset of OSA with obstructive and mixed apneas associated with bradycardia and asystole lasting up to 11 seconds. (C, central; ECG, electrocardiogram; EMG, electromyogram; IC, intercostal electromyogram; LL, left let; LOC, left outer canthus; NA, nasal airflow; O, occipital; OA, oral airflow; ROC, right outer canthus; T, Temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Berger A. Transient obstructive sleep apnea and asystole in association with presumed viral encephalopathy. *Neurology* 2003;60:1692–1694; Figs. 1 and 2, with permission.)



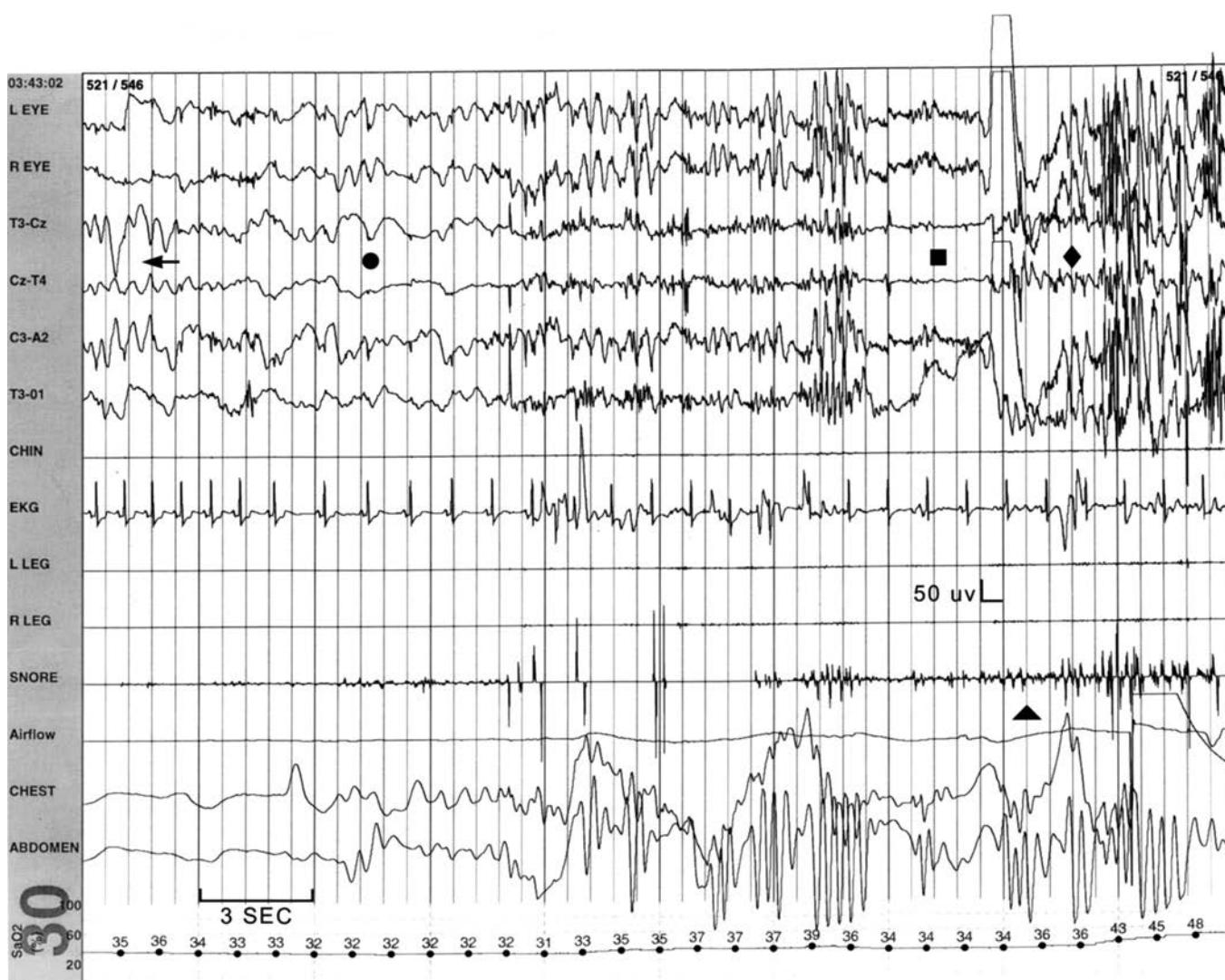
**Figure 11-10.** A PSG tracing (paper speed 10 mm/s) has been reduced to correspond to a temporally related microneurographic tracing (Fig. 11-11; paper speed 5 mm/s). Arrows indicate a prolonged mixed apnea of approximately 26-second duration occurring during REM sleep, associated with severe oxygen desaturation. (C, central; EMG, electromyogram; ET, ears tied; LOC, left outer canthus; N, nasal airflow; O, occipital; OA, oral airflow; ROC, right outer canthus; T, temporal; TM, thoracic movement.) (From Dyken ME. Cerebrovascular disease and sleep apnea. In: Bradley DT, Floras JS, eds. *Sleep Disorders and Cardiovascular and Cerebrovascular Disease*. Marcel Dekker, 2000:285–306; Fig. 2, with permission.)



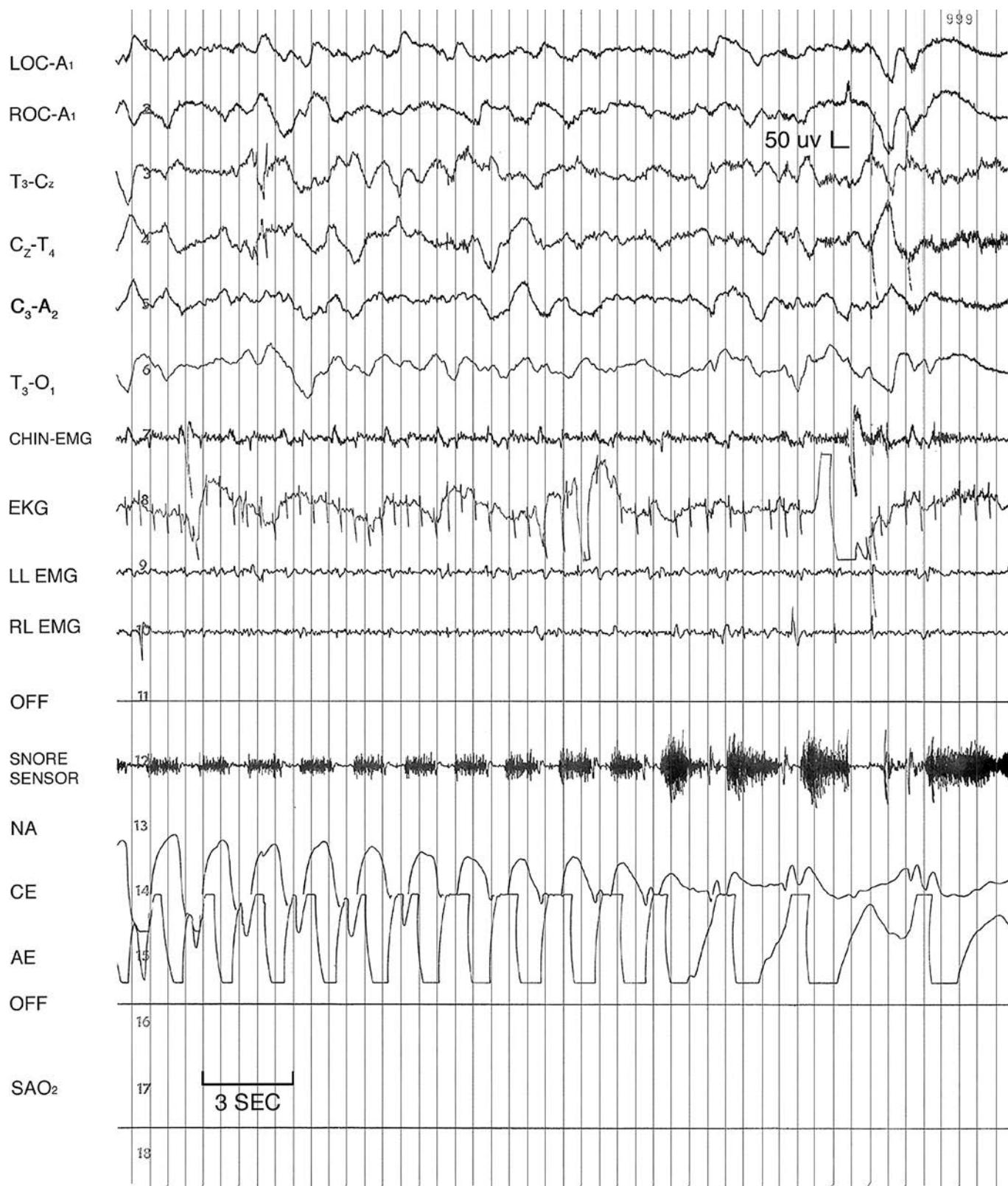
**Figure 11-11.** The arrows in this microneurographic tracing recorded from the peroneal nerve indicate a gradual elevation of efferent nerve activity during a mixed apnea. The activity peak is immediately followed by cessation of the apnea, with a subsequent marked elevation of arterial blood pressure to 215/130 mm Hg from a baseline of 135/80 mm Hg. MSNA, muscle sympathetic nerve activity; Pneu, chest excursion; Finapress; fingertip blood pressure. (From Dyken ME. Cerebrovascular disease and sleep apnea. In: Bradley DT, Floras JS, eds. *Sleep Disorders and Cardiovascular and Cerebrovascular Disease*. Marcel Dekker, 2000:285–306; Fig. 3, with permission.)



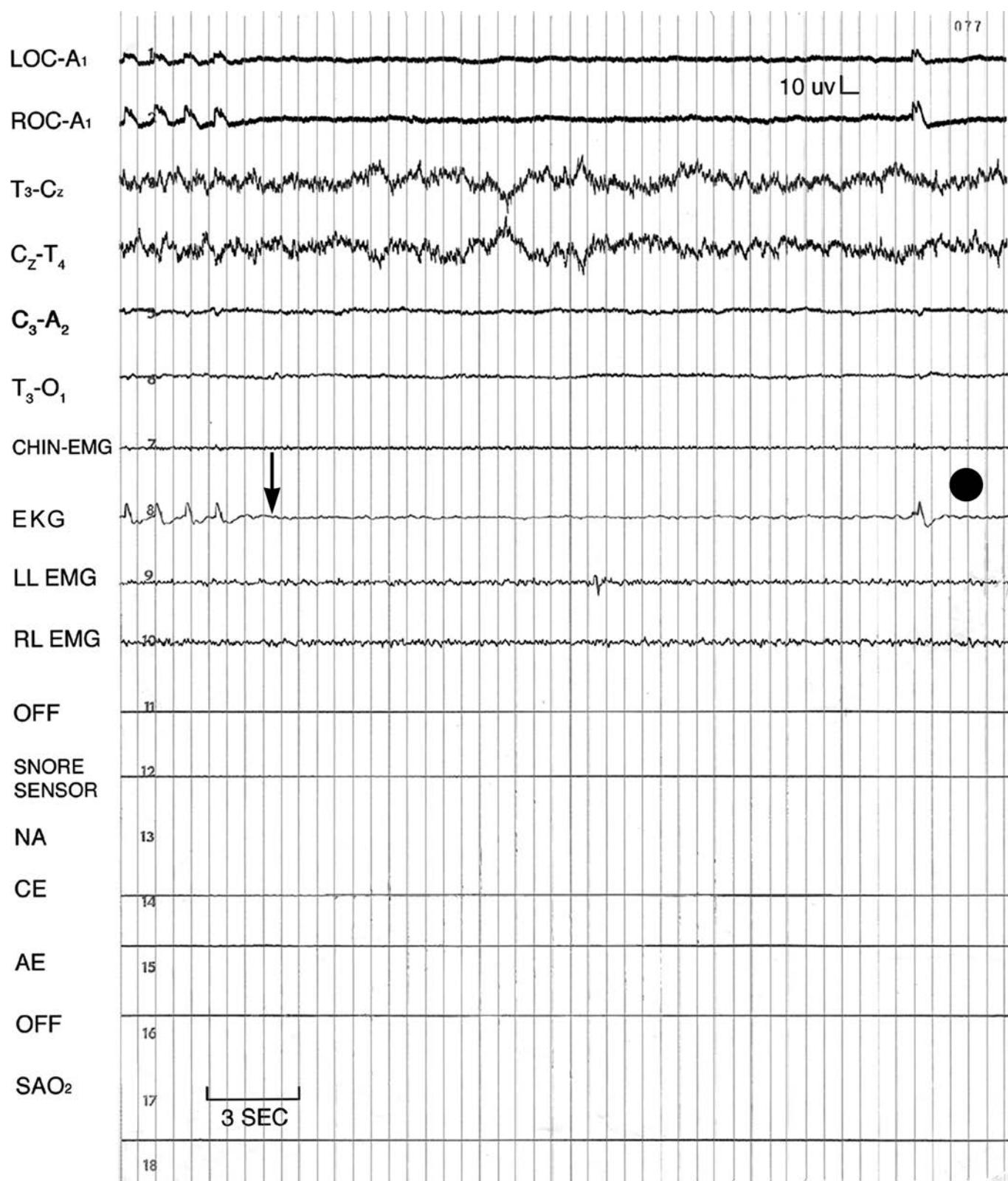
**Figure 11-12.** A previously healthy, 32-year patient with viral encephalitis and delirium alternating with stupor suffered the apparent new of OSA with obstructive and mixed apneas (see Fig. 11-9) associated with bradycardia and asystole lasting up to 11 seconds. These EKG findings led to emergent CPAP therapy, which at 8.0 cm of water pressure (cwp) provided resolution of all apneic events. (C, central; ECG, electrocardiogram; EMG, electromyogram; IC, intercostal electromyogram; LL, left let; LOC, left outer canthus; NA, nasal airflow; O, occipital; OA, oral airflow; ROC, right outer canthus; T, Temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Berger A. Transient obstructive sleep apnea and asystole in association with presumed viral encephalopathy. *Neurology* 2003;60:1692–1694; Fig. 2, with permission.)



**Figure 11-13.** Our patient, upon whom treatment for OSA was an option, suffered a prolonged obstructive apnea, which eventually resulted in a sudden EEG change from a classic REM sawtooth pattern (see arrow) to a poorly organized, diffuse delta slow-wave pattern (see closed circle), followed by a general flattening of all activity (see square) that led to attempts to arouse the patient (as evidenced by diffuse movement artifact; see diamond). Nevertheless, persistent obstruction (see triangle) necessitated emergency rescue breathing maneuvers. Persistent EEG flattening followed by slowing and eventual recover of normal waking patterns was appreciated in subsequent epochs. (L, left; R, right; T, temporal; C, central; O, occipital; CHIN, mentalis EMG; L LEG, left anterior tibialis EMG; R LEG, right anterior tibialis EMG; SNORE, snoring microphone; Airflow, nasal airflow; CHEST, thoracic respiratory effort; ABDOMEN, abdominal effort; SaO<sub>2</sub> (%), oxygen saturation.) (From Dyken ME, Yamada T, Glenn CL, et al. Obstructive sleep apnea associated with cerebral hypoxemia and death. *Neurology* 2004;62:491–493; Fig. 1, with permission.)



**Figure 11-14.** An 80-year-old man with multiple medical problems, who was admitted with exacerbation of pulmonary and cardiac disease under a do-not-resuscitate/do-not-intubate status (for whom sign consent had been given for PSG as part of an IRB approved study) had a 30-second obstruction that was associated with a S<sub>AO</sub><sub>2</sub> low of 12%. At that time, the EEG showed progressive development of a disorganized slow-wave pattern over a 2½-minute period, followed by ECS (using a recording sensitivity of 1.0  $\mu$ V/mm). (A<sub>1</sub>, left ear reference; A<sub>2</sub>, right ear reference; AD, abdominal effort; C, central; CE, chest effort; LL, left leg; LOC, left outer canthus; NA, nasal airflow; O, occipital; RL, right leg; S<sub>AO</sub><sub>2</sub>, oxygen saturation; T, temporal.) (From Dyken ME, Im KB. Sleep-disordered breathing and stroke. In: Silber MH, ed. *Sleep Medicine Clinics: Neurologic Disorders and Sleep*. Elsevier, Inc., 2008:3, 370; Fig. 7, with permission.)



**Figure 11-15.** After our patient (upon whom no heroic therapeutic interventions were allowed) had a final series of apneic events, no discernible EEG activity was captured while utilizing a recording sensitivity of  $1.0 \mu\text{V}/\text{mm}$ . A prolonged period of asystole (see arrow) was followed by cardiac arrest, at which time the patient was declared dead (see closed circle). (A<sub>1</sub>, left ear reference; A<sub>2</sub>, right ear reference; AD, abdominal effort; C, central; CE, chest effort; LL, left leg; LOC, left outer canthus; NA, nasal airflow; O, occipital; RL, right leg; S<sub>AO</sub><sub>2</sub>, oxygen saturation; T, temporal.) (From Dyken ME, Yamada T, Glenn CL, et al. Obstructive sleep apnea associated with cerebral hypoxemia and death. *Neurology* 2004;62:491–493; Fig. 2, with permission.)

## SUMMARY

A fundamental knowledge concerning the basic anatomy and physiology of central wake/sleep and breathing mechanisms helps explain the close relationship between neurological disease and some sleep problems, and provides a rational clinical approach to major sleep disorders such as narcolepsy and OSA. In narcolepsy with cataplexy, the identification of waking centers localized to the brainstem has allowed specific pharmacologic interventions utilizing medications that mimic the effects of endogenous monoaminergic and cholinergic neurotransmitters.

New research suggests narcolepsy with cataplexy and possibly other sleep disorders result from a genetic predisposition to autoimmune disease.<sup>20,21,35</sup> Aberrant genetic coding of elements in the respective hypocretin/orexin and peri-LC systems could allow for susceptibility to inducible (possibly virally mediated) changes, which leave cells prone to autoimmune attack. As such, genetic screening of high-risk individuals might eventually rationalize prophylactic immunosuppression, whereas neuronal transplantation may prove beneficial in cases where the disease has already taken hold.

Finally, OSA cohort studies have suggested early intervention with CPAP may prevent cerebral hypoxemia and stroke. If future clinical trials can prove the cost effectiveness of diagnosing and treating OSA after stroke, routine screening and more aggressive treatment options might become standard of care.

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# Technology of Polysomnography

## INTRODUCTION

The polysomnogram (PSG) is the diagnostic tool used for defining sleep and monitoring the major electrophysiologic changes that can occur during sleep. The term “polysomnography” was coined in 1974 by Dr. Jerome Holland from Stanford University after respiratory and cardiac monitoring were included as part of the standard recording parameters of an all-night sleep study.<sup>1</sup>

The PSG is the gold standard for evaluating many disorders of sleep and wakefulness, particularly sleep-disordered breathing. PSGs are performed in Sleep Disorders Centers that are either hospital based or free-standing. The studies are performed by trained technologists or technicians who work under the direction of a physician who specializes in sleep medicine. The standard recording analysis includes the following parameters: electroencephalography (EEG), electrooculography (EOG), electromyography (EMG) of the chin and anterior tibialis muscles, electrocardiography (ECG), nasal/oral airflow and pressure, chest and abdominal respiratory effort, oxygen saturation, and body position.<sup>2</sup> This chapter will address standard polysomnography, sleep stage scoring in the adult population, and the scoring of periodic limb movements in sleep (PLMS).

## THE TECHNOLOGISTS’ ROLE IN THE SLEEP LAB

Polysomnographic Technology has emerged as a distinct multi-disciplinary allied healthcare occupation. Polysomnographic technologists are trained to perform diagnostic procedures, frequently with therapeutic interventions, in the evaluation of a variety of sleep-related disorders. The duties of a technologist in the Sleep Center may vary depending on the size of the sleep lab, the shift (day, evening, or night) they are assigned to, and the number of laboratory personnel.

The polysomnographic technologist should be able to interact with patients in a calm, professional manner and be capable of clearly explaining the testing procedures and therapeutic interventions. They should be knowledgeable of the basic physiology associated with sleep and arousal disorders and be able to recognize when therapeutic or medical interventions are necessary. The technologist must be competent in the use of all instrumentation used in the sleep laboratory and is responsible for the integrity of the recording throughout the night. They must also be prepared to work 10 to 12 hour shifts during the

night time hours and remain vigilant during that time. The following are duties that one could expect to perform as a PSG technologist<sup>3,4</sup>:

- Review physician orders and the medical record.
- Set up and calibrate equipment.
- Interview the patient.
- Measure and apply electrodes and respiratory monitors.
- Perform physiologic calibration.
- Monitor acquisition of PSG data.
- Perform positive airway pressure (PAP) and oxygen titrations.
- Perform mean sleep latency testing (MSLT) and maintenance of wakefulness testing (MWT).
- Recognize and document clinical and physiologic events.
- Respond to emergencies.
- Provide patient education.
- Score studies and generate a report for physician interpretation.
- Schedule patients.
- Participate in quality assurance activities.
- Archive data.
- Participate in continuing education.
- Participate in research.

Training in sleep technology can be obtained through a CAA-HEP (Commission on Accreditation of Allied Health Program)-accredited Polysomnographic Technologist Training program or an Electroneurodiagnostic (END) or Respiratory Therapy program with an add-on track for Polysomnography. The American Academy of Sleep Medicine (AASM) also offers training through online self-study modules called *A-STEP*. A technician who chooses to pursue polysomnographic technology as a career should consider becoming credentialed by the Board of Registered Polysomnographic Technologists (BRPT). Once a technician completes the required training and meets the eligibility criteria (Table 12.1), they may sit for the exam and gain the recognition of Registered Polysomnographic Technologist (RPSGT).<sup>5</sup>

## PREPARING FOR THE PATIENT

A sleep center should provide an inviting home-like environment in an attempt to make the patient as relaxed as possible. Often times, the bedrooms are equipped with comfortable furniture, private bathrooms, and cabinetry that hide necessary medical equipment such as oxygen flow meters and PAP equipment.

<b>TABLE 12.1</b> Eligibility Requirements for PSG Boards			
<i>Pathway 1</i>	<i>Pathway 2</i>	<i>Pathway 3</i>	<i>Pathway 4</i>
18 mo experience with PSG recording/scoring	6 mo experience with PSG recording/scoring	Complete a CAAHEP accredited polysomnographic technology program (stand alone or add-on)	9 mo experience with PSG recording/scoring
Complete AASM A-STEP Self-Study Modules (or BRPT designated alternate educational program) Proof of completing secondary education	Must hold a credential, including: R. EEG T., R.EP T., PhD., MD, DO, or RT. (see website for full listing)		Completion of BOTH the AASM A-STEP Introductory Course and the AASM A-STEP Self-Study Modules (or a BRPT designated alternate educational program) Proof of completing secondary education

*Source:* Adapted from the Board of Registered Polysomnographic Technologists (BRPT) website. Please refer to the website for a full description of the requirements. [http://www.brpt.org/Exam\\_info/eligibility.htm](http://www.brpt.org/Exam_info/eligibility.htm)

For efficiency and safety, a centralized technologist control room should be within close proximity of the bedrooms.

### REVIEW OF THE PHYSICIAN'S ORDER

The technologist should begin by reviewing the physician's order. The order should describe the patient's primary complaints, the suspected and differential diagnoses, and the type of study requested. The technologist should be alert for special instructions such as the need for oxygen therapy or use of a seizure montage. If clarification regarding the order is needed, it is best to obtain information from the referring physician or the sleep center's medical director during the day.

### REVIEW OF THE MEDICAL RECORD

The referring physician should have clearly documented in their clinical history a justification for the sleep laboratory referral. In addition, the technologist should review the medical record for important information that might be gleaned from previous PSG studies, EKG reports, laboratory values [including arterial blood gas (ABG)], or notes regarding any recent hospital admissions. Although a list of the patient's current medications should be available in the medical record, it is important to review this list with the patient for accuracy as many drugs can affect the appearance of the EEG and adversely affect sleep. The medical record is also useful in identifying patients with special needs so that accommodations for the PSG can be individualized.

### PREPARING FOR HOOKUP

The technologist should ensure that the hook-up area and the patient's bedroom are clean and orderly prior to the patient's arrival. Prepare ahead for special accommodations such as a cot for a caretaker. Necessary supplies for hookup should be laid out and ready for use. Monitoring cables and equipment in the bedroom should be organized and out of sight if possible. Being organized will make the hook-up process more efficient and put the patient at ease.

### SELECTING A MONTAGE

After reviewing the physician's order and the patient's medical record, the montage must be selected. It is important to select a montage that will include all parameters necessary to diagnose the specific sleep/wake disorder in question. Your sleep center should have several preprogrammed montages to choose from. The medical director may determine which montage is to be used; however, a trained technologist should be able to make this decision. Montage selection is fairly straightforward. For example, there should be a montage for routine diagnostic PSGs (Table 12.2), a montage for PAP trials, a seizure montage with added EEG derivations, and perhaps a montage with extra limb leads or end-tidal CO<sub>2</sub>. Sensitivity and filter settings are programmed and may be adjusted once the study begins.

### CALIBRATION

Although some believe that amplifier calibrations are no longer needed when using digital equipment, the AAST's Technical Guideline for Standard Polysomnography recommends amplifier calibrations at the beginning and end of a study.<sup>6</sup> Most systems have a calibration montage in which all channels have identical settings and a 50-μV signal is introduced allowing the technologist to quickly ensure that the signal polarity, amplitude, and filter settings in each channel are identical (see page 36, "Calibration signal" in *Practical Guide: EEG*). Once the all channel calibration has been performed, select the study montage and apply another calibration signal to verify the appropriate change in signal response.<sup>6,7</sup> Calibrations for any appropriate ancillary equipment should be performed routinely as well.

### AFTER PATIENT ARRIVES

#### ORIENTATION

The first encounter with the patient is crucial as this is where the technologist/patient relationship begins. The more comfortable the patient is made to feel from the beginning, the more relaxed they are apt to be at bedtime and throughout the study. During this time, the patient should be oriented to their

<b>TABLE 12.2</b>	<b>PSG Montage and Parameter Settings</b>				
<i>Label</i>	<i>Inputs</i>	<i>Sensitivity (μV/mm)</i>	<i>HFF (Hz)</i>	<i>LFF (Hz)</i>	<i>Sampling Rate (Hz)</i>
Right Frontal EEG	F4-M1	7	35	0.3	200–500
Right Central EEG	C4-M1	7	35	0.3	200–500
Right Occipital EEG	O2-M1	7	35	0.3	200–500
Left EOG	E1-M2	7	35	0.3	200–500
Right EOG	E2-M2	7	35	0.3	200–500
Chin EMG	Chin 1–Chin 2	2	100	10	200–500
ECG Lead	ECG 1–ECG 2	20	70	0.3	200–500
Left Leg EMG	L leg 1–L leg 2	7	100	10	200–500
Right Leg EMG	R leg 1–R leg 2	7	100	10	200–500
Snore	Snore	7	100	10	200–500
Thermal Flow	Airflow	Variable	15	0.1	25–100
Pressure Flow	Pressure	Variable	15	0.1	25–100
Thoracic Effort	Respiratory	Variable	15	0.1	25–100
Abdominal Effort	Respiratory	Variable	15	0.1	25–100
Oximetry (SpO <sub>2</sub> )	DC	N/A	N/A	N/A	10–25
Body Position	DC	N/A	N/A	N/A	1

*Source:* Adapted from The AASM Manual for the Scoring of Sleep and Associated Events. Filter settings may vary according to the manufacturer's specifications. Sensitivity settings for ECG and respiratory channels should be adjusted during biocalibrations to display optimal signals and may need to be adjusted during the study.

bedroom, bathroom, and any other area they may need to access such as a lounge or snack area. Instructions should be given for use of the television, bed remote, fan, thermostat, etc.

## QUESTIONNAIRES

Many sleep centers mail a Sleep History Questionnaire to patients and ask that they bring it with them the day of their test. The technologist should review the questionnaire to ensure that it is complete. The patient should also be given a Pre-sleep Questionnaire to complete prior to bedtime (Fig. 12-1).<sup>8</sup> This questionnaire typically addresses the most recent sleep habits or events and provides an update of the medication regimen.

## INTERVIEW

The technologist should discuss the sleep questionnaire with the patient and ensure that it is filled out completely. The medical history should also be reviewed and confirmed for accuracy making note of any changes in the patient's medical condition since they were last seen by the referring physician. Here are common questions that should be addressed regarding the patient's sleep habits:

- What is your routine bedtime and awakening time?
- How long does it take you to fall asleep?
- Do you snore?
- Do you have frequent arousals in the night? How many and for what specific reasons?
- Do you wake up choking or gasping for air?
- Do your legs jerk at night?
- Do you sleepwalk or act out your dreams?
- Do you feel unrefreshed in the morning?
- Do you have a headache in the morning?
- Do you feel excessively sleepy during the day?
- When questioned does the patient describe hypnagogic hallucinations, sleep paralysis, or cataplexy?

After discussing the medical and sleep history, the technologist should explain the testing procedure and potential therapeutic interventions and allow time for questions.

## CONSENT FORMS

Once the procedure has been explained to the patient, consent forms can be discussed and signed. These forms will vary from lab to lab. Our "Consent for Operation or Procedure" form documents the patient's consent to video/audio recording as well as to the potential use of continuous positive airway pressure therapy (CPAP). This form becomes a permanent part of the patient's medical record.

## ELECTRODE AND SENSOR APPLICATION

Electrode and sensor placement and application are very important in determining the quality of the recording. Careful preparation and placement will help to ensure an accurate recording and minimize the need to disrupt the patient during the study. All scalp and body electrode sites should be prepared using an abrasive cleaning gel prior to attaching the electrodes. Impedance for EEG and EOG electrodes should not exceed 5 K ohm.<sup>6</sup> After all the electrodes are in place and impedances are at an acceptable level, the wires should be grouped into a "pony tail" using tape or Velcro straps to keep the patient from getting tangled and to minimize electrical interference.

## PLACEMENT AND APPLICATION

### EEG

Sleep staging and documentation of arousals are identified primarily by the EEG recording. Three channels of EEG, representing the frontal (F<sub>z</sub>), central (C<sub>z</sub>), and occipital (O<sub>z</sub>) regions

**Pre-Sleep Questionnaire**

PSG Date \_\_\_\_\_

Name \_\_\_\_\_ Hospital# \_\_\_\_\_ Age \_\_\_\_\_ Night# \_\_\_\_\_

1. How much sleep did you have last night? \_\_\_\_\_
  2. Was this amount of sleep the same \_\_\_\_\_, more \_\_\_\_\_, or less than your usual sleep?
  3. Did you nap today? \_\_\_\_\_ yes \_\_\_\_\_ no. What time? \_\_\_\_\_ How long? \_\_\_\_\_
  4. When did you eat last? \_\_\_\_\_ Did you eat the same \_\_\_\_\_, more \_\_\_\_\_, or less \_\_\_\_\_ than usual?
  5. Do you feel ill or different than usual right now? \_\_\_\_\_ If so, explain briefly.
  
  6. Describe your level of alertness (circle one):
    - a. Alert
    - b. Relaxed
    - c. Slowed down
    - d. Sleepy
    - e. Very sleepy
    - f. Fighting sleep.
  7. What is your usual bedtime? \_\_\_\_\_
  8. What time do you awaken in the morning? \_\_\_\_\_
  9. List all of your medications taken today.

<u>Medication</u>	<u>Amount</u>	<u>Medication</u>	<u>Amount</u>
_____	_____	_____	_____
_____	_____	_____	_____
10. When did you last take any medication to help you sleep or to keep you awake?  
Date: \_\_\_\_\_ Medication: \_\_\_\_\_
11. Have you ever had a tonsillectomy? \_\_\_\_\_ adenoidectomy? \_\_\_\_\_
12. Add any additional comments here:

**Epworth Sleepiness Scale**

In contrast to just feeling tired, how likely are you to doze off or fall asleep in the following situations? (Even if you have not done some of these things recently, estimate how they would affect you.) Use the following scale to choose the most appropriate number for each situation:

- 0 = Would never doze  
 1 = Slight chance of dozing  
 2 = Moderate chance of dozing  
 3 = High chance of dozing

<b>SITUATION</b>	<b>CHANCE OF DOZING</b>
Sitting and reading	
Watching T.V.	
Sitting inactive in a public place (ie. theater)	
As a car passenger for an hour without a break	
Lying down to rest in the afternoon	
Sitting & talking to someone	
Sitting quietly after lunch without alcohol	
In a car, while stopping for a few minutes in traffic	
<b>TOTAL SCORE</b>	

**Figure 12-1.** The Presleep questionnaire used at the University of Iowa Hospital. The form is completed the night of the study prior to lights out. The Epworth Sleepiness Scale is included as a method to assess the patient's subjective daytime sleepiness.

referenced to the contralateral mastoid ( $M_1$ ), should be recorded.<sup>2</sup> Backup electrodes ( $F_3$ ,  $C_3$ ,  $O_1$ ,  $M_2$ ) are also applied to avoid interrupting the study should a malfunction with the primary electrodes occur during the study. The EEG electrodes should be placed according to the International 10-20 System of electrode placement.<sup>9</sup> Gold or silver-silver chloride electrodes can be attached with either collodion or paste. However, since the PSG is a relatively long recording and patients may make multiple position changes during the night, collodion is a more secure application method and will help prevent artifact and the need to reattach electrodes during the night.

Sensitivities and filter settings are preprogrammed but can be adjusted if needed during the study. Sensitivities that provide a deflection of 7.5 to 10 mm/50  $\mu$ V signal for EEG and EOG channels are preferred. A high-frequency filter of 35 Hz allows the necessary waveforms to be recorded but at the same time reduces high-frequency interference. A low-frequency filter of 0.3 Hz will allow the slower frequencies during N3 as well as rapid and slow eye movements to be appreciated.

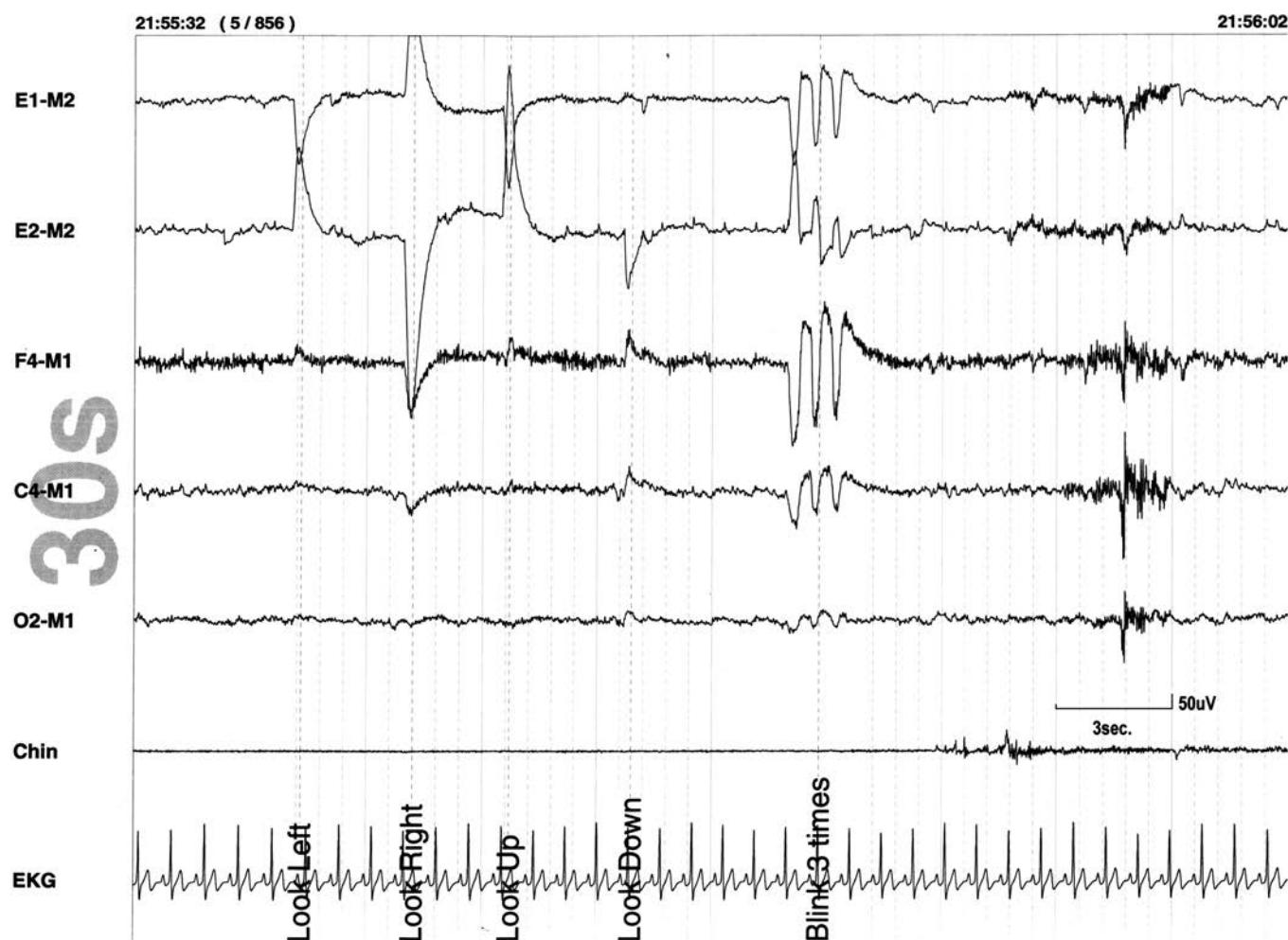
### EOG

The electrooculogram records vertical and horizontal eye movement and assists in identifying sleep onset and the differentiation

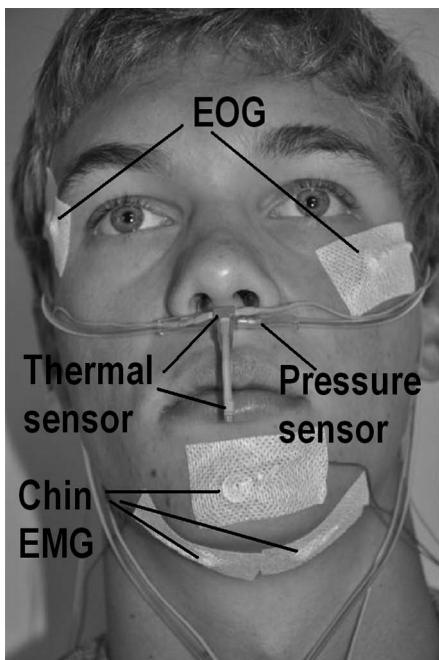
of sleep stages. The cornea (front of the eye) has a positive charge compared to the retina (back of the eye). When the patient looks toward one of the eye leads (E1 or E2), a positive charge is created and a downward deflection in the channel is recorded (when E1 or E2 is in input 1). At the same time, a negative charge is being recorded by the opposite eye lead causing an upward deflection. As such, horizontal and vertical eye movements are displayed as out-of-phase signals in the eye lead channels (Fig. 12-2; see also *Practical Guide: EEG*, Chapter 14 and Figs. 14-3 through 14-13). The morphology and duration of the eye movements help to discern the stages of sleep, particularly Stage R (REM) sleep and the transition from awake to Stage N1.

The EOG leads should be applied using disposable self-adhesive surface electrodes or silver-silver chloride electrodes attached with tape. Care should be taken when prepping the area as the skin around the eyes tends to be thin and sensitive. The recommended placement for the EOG electrodes is as follows (Fig. 12-3):<sup>2</sup>

- E1 (left eye)—1 cm *below* the left outer canthus of the eye.
- E2 (right eye)—1 cm *above* the right outer canthus of the eye.
- Both E1 and E2 should be referenced to the same mastoid electrode.



**Figure 12-2.** As an initial calibration, the patient is asked to look left, right, up, down, and blink 3 times. With this eye monitor derivation (shown in Fig. 12-3), eye movements are registered by out-of-phase relationship between channels 1 and 2 irrespective of the direction of eye movements.



**Figure 12-3.** E1 and E2 electrode locations for monitoring eye movements. Three electrodes are applied to record submental (chin) EMG activity. One of the electrodes below the inferior edge of the mandible will serve as a backup. The thermal sensor is “piggy-backed” to the nasal pressure cannula.

### Submental EMG

The submental (chin) EMG recording is very important for determining sleep onset and stage R sleep. As the patient drifts to sleep, there should be a reduction in the amplitude of the muscle activity from the baseline. During stage R sleep, the chin EMG typically is at the lowest amplitude of the night. This channel may also assist in identifying arousals.

Three electrodes should be securely applied to record chin EMG. Gold or silver-silver chloride electrodes applied using collodion is the most secure method for attaching these electrodes; however, tape may be used as well. Impedance for EMG channels should not exceed  $10\text{ k}\Omega$ .<sup>6</sup> The recommended placement for the submental EMG electrodes is as follows (see Fig. 12-3):<sup>2</sup>

- One electrode in the midline 1 cm above the inferior edge of the mandible (mental)
- One electrode 2 cm below the inferior edge of the mandible and 2 cm to the right of the midline (submental)
- One electrode 2 cm below the inferior edge of the mandible and 2 cm to the left of the midline (submental)

The standard recording should reference one of the electrodes below the mandible to the electrode above the mandible. The third electrode below the mandible will act as a backup.

A sensitivity of  $2\text{ }\mu\text{V/mm}$  typically provides an optimal recording that allows comparisons in the EMG level between awake, non-REM, and REM sleep. The high-frequency filter will allow the necessary muscle activity to pass when set at 100 Hz. To avoid interference from slow activity, the low-frequency filter should be set at 10 Hz.

### Lower Extremity EMG

Abnormal limb movements at night are identified during the PSG by recording muscle activity from electrodes applied to the anterior tibialis muscle of the lower limbs. When these electrodes capture repetitive, periodic movements, it is often indicative of *Periodic Limb Movement Disorder (PLMD)*; a relatively frequent problem that can be diagnosed in the sleep laboratory.

To locate the anterior tibialis muscle, the technologist should ask the patient to dorsiflex their foot after which the muscle can easily be located along the lateral side of the tibia. Two electrodes should be applied 2 to 3 cm apart longitudinally on the belly of the muscle (Fig. 12-4). It is preferable to record from both legs separately.<sup>2</sup> Standard EEG electrodes can be applied with collodion, or disposable self-adhesive surface electrodes can be used. The wires should be anchored with extra tape and a stress loop to secure the leads. It is also helpful if the electrodes are fed through the patient’s bed clothes to avoid the patient getting tangled in the wires during the night.

### ECG

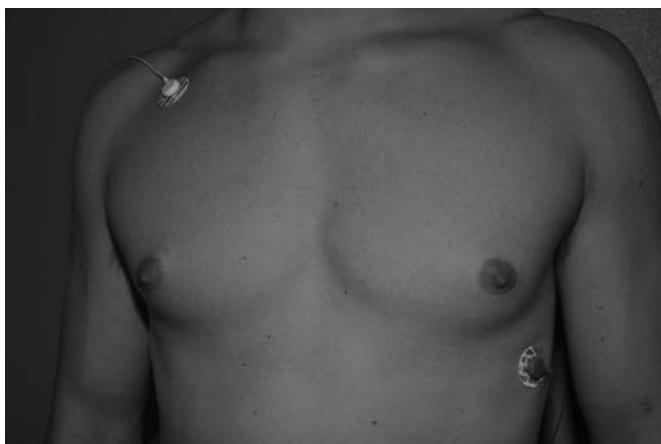
A single-channel, modified Lead II recording with standard ECG (peel and stick) electrodes is recommended to record basic heart rate and arrhythmias during the PSG.<sup>2</sup> One electrode is placed on the chest below the right clavicular bone and a second electrode should be aligned in parallel to the left hip in the 6th intercostal space (Fig. 12-5). Recording and careful monitoring of the ECG is crucial to ensure the patient’s safety during the study. Often times, ECG abnormalities are not documented in the patient’s history as they may only occur while the patient is sleeping and may be noted for the first time during the PSG. Thus, the technologist should be trained to recognize not only normal ECG patterns, but also arrhythmias, and be prepared to respond to cardiac emergencies.

### Airflow

Airflow monitoring helps to detect and differentiate sleep-related breathing disorders that are frequently encountered in



**Figure 12-4.** Lower limb movements are recorded by placing two electrodes on the anterior tibialis muscle of each leg. A stress loop is taped above the electrodes for added security.



**Figure 12-5.** ECG electrodes are placed to record a modified Lead II derivation. One electrode is placed below the right clavicle bone and a second lead is located above the left hip in the 6th intercostal space.

the sleep laboratory. Two separate airflow channels using different recording methods are recommended. Apneas are identified by using an oral-nasal thermal sensor, while hypopneas are detected with the use of an oral-nasal air pressure transducer.<sup>2</sup>

The *thermal sensor* (thermistor or thermocouple) is a qualitative measurement that reflects temperature changes between the room air and the patient's expired air. This sensor is recommended to detect apneas and is not considered reliable for the detection of hypopneas. The sensor is placed above the upper lip with the nasal prongs placed close to the nares to capture air flow from the nose, while the third prong is situated in front of the mouth (see Fig. 12-3). Most sensors are pliable and can be bent for optimal placement. The tips of the sensors should not touch the skin. The sensor should be secured to the face with tape to avoid undue movement and the wire bundled behind the head. Several situations can cause a suboptimal airflow signal; the sensor becomes wet or displaced, the room is too warm (minimizing the temperature difference between the exhaled and the room temperature air), and air is blown over the patient's face by a room fan or CPAP machine.

The *nasal pressure transducer* measures the volume of air expired through an oral-nasal cannula and converts that measurement into an electrical signal that is subsequently recorded as an airflow signal. This is the recommended device for detection of hypopneas and *respiratory effort-related arousals (RERA)*. The nasal/oral cannula is positioned on the upper lip, much like an oxygen cannula (see Fig. 12-3). The nasal prongs should rest just inside the nares and the oral prong should lie between the upper and lower lips. If either cannula is too long, they may be trimmed to avoid contact with mucus that may block the lumen and to improve patient comfort.

### Chest and Abdominal Respiratory Effort

Monitoring of respiratory effort is also essential in clearly distinguishing the different sleep-related breathing disorders. The recommended method for monitoring respiratory effort is calibrated or uncalibrated *inductance plethysmography* or *esophageal manometry*,<sup>2</sup> although the latter is not routinely used in the clinical setting.

Inductance plethysmography belts are designed to monitor actual movements of ventilation. A small current is applied to wires that are woven throughout the length of a belt-like band, and as the band stretches with inhalation and exhalation, changes in capacitance produce a semiquantitative signal.<sup>10</sup> The belts must be specifically placed where there is maximal respiratory movement in order to capture the best possible signal. As maximal ventilatory excursion of the rib cage is appreciated below the fourth or fifth intercostal spaces, the thoracic belt should be placed just below the pectoral muscle and either above or on the xiphoid process. The pectoral muscle helps prevent the belt from slipping up into the armpits. The abdominal belt should be wrapped around the patient near the umbilicus (navel) (Fig. 12-6).<sup>11</sup> The belts should be snug but not too tight or too loose as either may cause inadequate signals.

### Snore Monitor

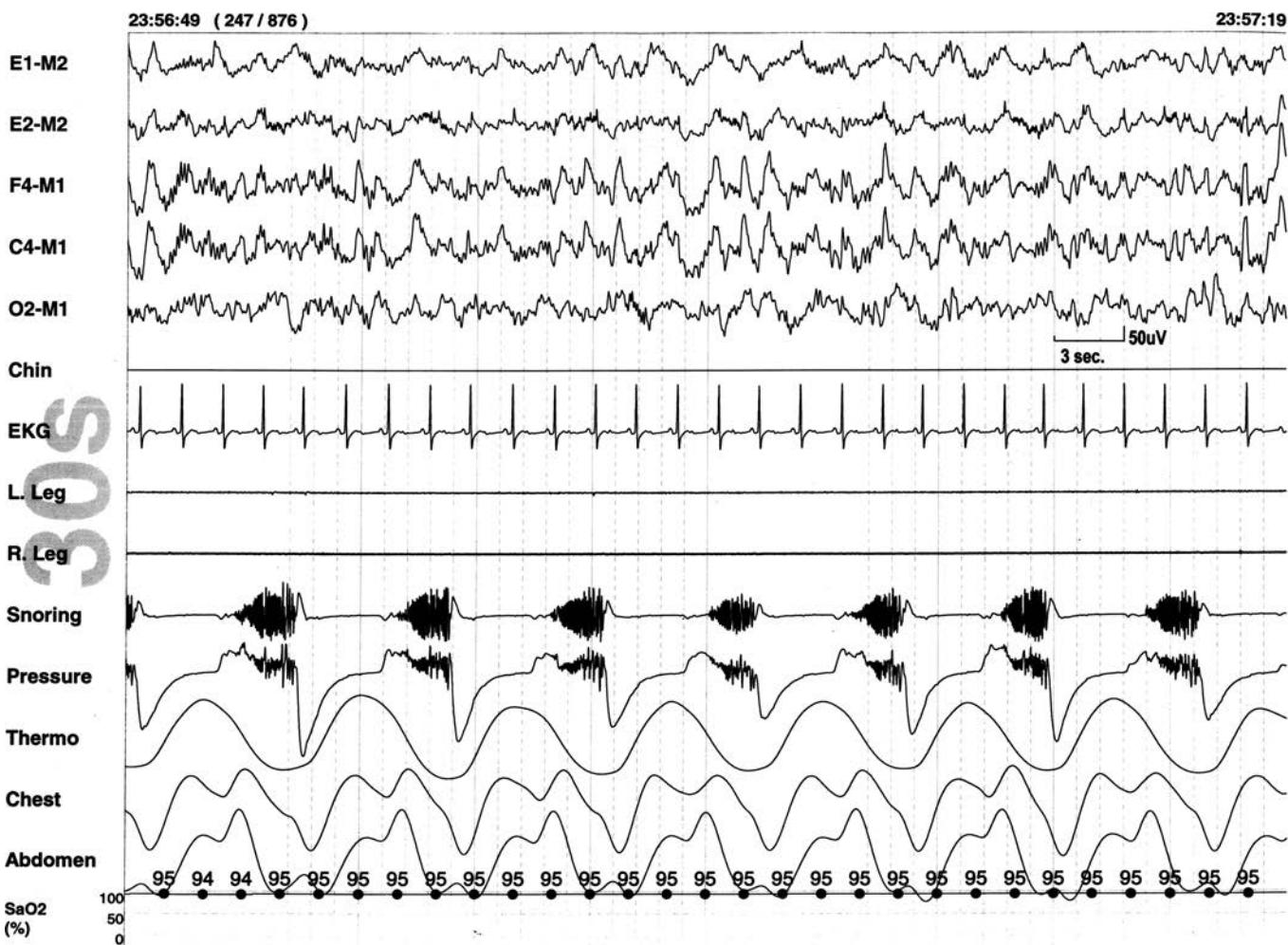
Snoring can be recorded several ways. A *snore sensor* records vibrations using a piezo crystal, which presents as a burst of fast activity that resembles a muscles discharge (Fig. 12-7). The sensor should be placed on the anterior aspect of the neck in a location where vibrations are most prominent; often at the level of the larynx (Fig. 12-8). To find the best location, place two fingers on the patient's throat and ask them to cough or hum. The site should be cleaned with rubbing alcohol, and the sensor taped to the neck. Less commonly used is the snore microphone, which records sound and should be placed where the snoring sound is best heard.<sup>12</sup> Some pressure transducer monitors are capable of monitoring snoring without adding extra sensors. The signal can be either superimposed on the airflow channel or recorded in a separate channel (see Fig. 12-7).

### Oximetry

Monitoring of the SpO<sub>2</sub> (oxygen saturation) is a vital part of the sleep study as it is used to define the severity of respiratory events as well as monitor the safety of the patient. The pulse oximeter is a DC device used to measure the SpO<sub>2</sub> or the



**Figure 12-6.** Respiratory effort is monitored using inductance plethysmography belts. The thoracic belt is placed just below the pectoral muscle and either above or on the xiphoid process. The abdominal belt is secured just above the umbilicus (navel).



**Figure 12-7.** Snoring artifact is appreciated in the snore channel as well as superimposed on the nasal pressure channel.

amount of saturated oxygen in the blood by using a light-emitting diode (LED) that shines a red and infrared light into the tissue bed of a finger. A photodiode on the opposite side of the sensor serves as a photodetector to determine the percentage of hemoglobin that is saturated by oxygen.<sup>13</sup> The sensor sends an electronic signal to the oximeter and the amount is displayed as a percentage, either linearly or numerically or both. The signal averaging time must be 3 seconds or less.<sup>2</sup>

Most oximeters offer several different types of sensors, i.e. reusable clips, reusable or semireusable sensors, or disposable sensors. The clip or sensor should preferably be applied to the index finger, but alternative fingers may be used if need be. Nail polish and acrylic nails should be removed prior to the study as they may reduce the amount of light transmitted through the nail bed.

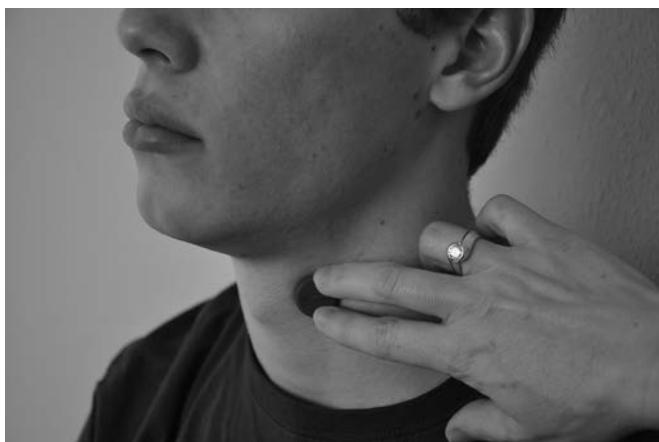
When placing the sensor on the finger, it is important to ensure that the light-emitting diode is on the top of the nail bed with the receiving diode on the finger pad opposite the LED (Fig. 12-9). Depending on the type of sensor used, tape may be used to secure the sensor. Care should be taken to apply tape either in a spiral motion or vertically to avoid cutting off circulation with tape that is wrapped horizontally around the finger. After the sensor is applied, ask the patient to bend their finger

down to add slack to the wire and apply another small piece of tape across the top of the hand to help secure the sensor.

There are several physiologic and nonphysiologic artifacts that can cause an inadequate oximetry recording. Movement may cause variations in vascular filling and cause the signal to drop out. Poor skin contact and poor vascular perfusion due to medical conditions will create a similar effect. In these situations, alternative recording sites would include a toe, an earlobe, or the forehead.

### Body Position

Precise body position monitoring is important in the diagnosis of sleep-disordered breathing and can be monitored with a body position sensor or by visual observation and documentation. A *body position sensor* may be attached to the center of the thoracic belt and recorded in a DC channel. The sensor typically detects supine, lateral, prone, and upright sleeping positions. Visual observation and documentation by the technologist should complement the position channel. Body position must be incorporated into the sleep report to allow for assessment of sleep-disordered breathing in relation to body position,<sup>6</sup> as the supine position (due to the effects of gravitation upon the



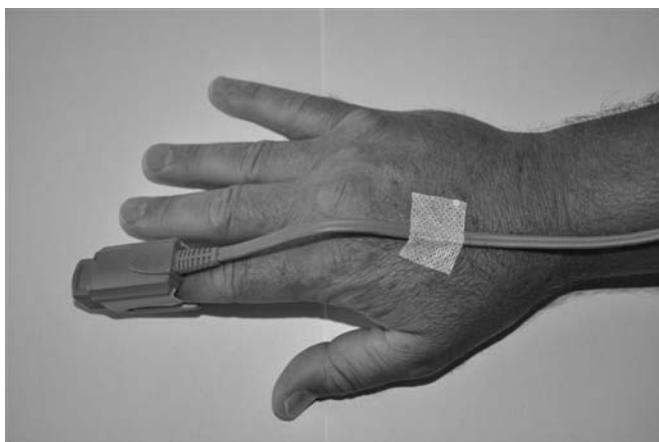
**Figure 12-8.** The snore sensor is placed on the anterior aspect of the neck where vibrations are most prominent.

oropharynx) tends to be frequently associated with more severe and frequent pathological events.

#### ADDITIONAL RECORDING PARAMETERS

Additional recording parameters may be added as deemed appropriate by the sleep center's medical director. *Capnography* is commonly used during pediatric studies to diagnose nocturnal hypoventilation, while for adults it can provide evidence suggestive of hypoventilation.<sup>2</sup> Capnography is the measurement of carbon dioxide ( $\text{CO}_2$ ) in an exhaled breath or in the blood depending on the recording method. *End Tidal  $\text{CO}_2$*  ( $\text{EtCO}_2$ ) monitoring is more commonly used during polysomnography and measures the peak concentration of carbon dioxide at the end of expiration via a nasal or an oral-nasal cannula. *Transcutaneous  $\text{CO}_2$*  ( $\text{TCO}_2$ ) monitoring records the amount of  $\text{CO}_2$  in the blood using a heated sensor applied to the skin.<sup>6</sup>

*Esophageal pressure* is measured by inserting a balloon-tipped catheter through the nasal passage into the esophagus where it detects pressure changes in the thoracic cavity. Although it is recommended for diagnosing *Upper Airway Resistance Syndrome* (*UARS*),<sup>2</sup> esophageal pressure monitoring is not routinely used



**Figure 12-9.** A reusable oximeter clip is placed on the index finger to measure  $\text{SpO}_2$ .

in sleep laboratories due to its relative invasive nature and concerns for patient comfort.<sup>14</sup>

At times, *Gastroesophageal Reflux Disease* (GERD) may occur as a result of increased intra-abdominal pressure generated during obstructive sleep apneic events.<sup>15</sup> *Esophageal pH monitoring* assesses the acidity levels in the esophagus using a catheter that is inserted through the nasal cavity into the esophagus. Although it is not commonly utilized in most sleep laboratories, in certain instances esophageal pH monitoring may provide insight in the evaluation of GERD in relation to a patient's sleep.

Recording of the *upper extremity limbs* is necessary for a thorough evaluation of *REM Behavior Disorder* (RBD) as well as to assess *Restless Legs Syndrome* and *Periodic Limb Movement Disorder* when a patient presents to the sleep laboratory with limb movements that affect the upper extremities. Upper extremity muscle activity can be recorded by applying two electrodes spaced 2 to 3 cm apart on the forearm flexor and extensor muscles of both arms.<sup>16</sup>

### THE RECORDING

After all pre-study questionnaires are completed, the appropriate montage is selected, and electrodes and sensors are attached, the patient will be ready for the formal PSG recording. The recording is generally performed at a paper speed of 10 mm/s or a digital screen display of 30 seconds.

### PHYSIOLOGIC CALIBRATIONS

This calibration exercise, also commonly known as "Biocalibrations" (not to be mistaken for the biocalibration performed during EEGs where an AC signal from the same two inputs is recorded in all channels), ensures electrode signal integrity and should be done at the beginning of each PSG prior to "Lights Out" (indicating the formal start of the PSG) and after "Lights On" (the formal end of the study).<sup>6</sup> The patient is asked to perform a series of tasks that will produce physiologic signals allowing the technologist to verify that the signal generated by the patient coincides with the appropriate electrographic changes on the polygraph (Table 12.3). For example, when the patient is asked to move their eyes, deflection in the eye lead channels should be appreciated; when asked to flex their foot, an increase in muscle activity from the appropriate leg channel should be noted (Fig. 12-10). Asking the patient to lie quietly with their eyes closed will establish the awake, resting baseline activity, which will assist with scoring and interpretation.

During the calibration, the technologist should assess for any technical problems. This will be the technologist's final chance to fix electrodes or sensors without interrupting the study. Remind the patient that if he/she needs to say anything, to speak out as he/she can be heard through the intercom. Once the technologist is satisfied with the recording, bid the patient a "good-night" and document "Lights Out" on the PSG recording.

### OBSERVATION AND DOCUMENTATION

Observation and documentation is essential to a successful study. Documentation begins with "Lights Out" and continues

**TABLE 12.3****Biocalibration Instructions**

<i>Calibration</i>	<i>Instructions</i>
Close Eyes	"Lie quietly and close your eyes." Record with eyes closed for 30 s to assess the awake, resting baseline activity.
Open Eyes	"Open your eyes and look straight ahead." Record for 30 s with eyes open. Alpha activity should attenuate when eyes open.
Look Right	"Without moving your head, look to the right." Assess for a rapid, out-of-phase signal in the eye lead channels
Look Left	"Look to the left."
Look Up	"Look up."
Look Down	"Look down."
Blink 5 times	"Look straight ahead and blink five times."
Clench Teeth	"Bite down and clench your teeth." A burst of muscle activity should be seen in the chin EMG channel
Flex Right Foot	"Flex your right foot." A burst of muscle activity in the right leg EMG channel should be noted.
Flex Left Foot	"Flex your left foot." A burst of muscle activity in the left leg EMG channel should be noted.
Snore Sound	"Make a snore sound or hum." A burst of muscle activity should be seen in the snore channel
Deep Breath, Hold	"Take a deep breath in and hold it." Have the patient hold his/her breath for a few seconds. The respiratory channels should be flat.
Breath Normal	"Exhale and breathe normally." Review the respiratory channels for an adequate airflow and effort signal.
Paradoxical Breathing	All three respiratory channels should be in-phase. "While holding your breath, move your chest and abdomen in and out as if trying to breathe." This should produce a flat line in the airflow channel and an out-of-phase signal between the thoracic and abdominal effort channels.

Biocalibration instructions are given at the beginning of the study prior to "lights out" and at the end of the study after "lights on." This calibration ensures the integrity of the recording.

in a chronological order until the end of the PSG. Video and audio recordings are required during the study for the patient's safety and to assist with the clinical evaluation. The technologist's adjunctive observations may also be very important for an accurate diagnosis. Adjusting the camera's lens in or out may help to identify subtle movements; however, at times it may be necessary for the technologist to enter the room in an attempt to provide a more accurate description of subtle sounds and behaviors that cannot be clearly appreciated on the video/audio system.

Occasionally, the patient's mental status may be in question. In these situations, the technician should document whether the patient is clearly alert and oriented to person (ask "What is your name?"), place (ask "Where are you?"), and time (ask "What is the date?"). The technologist can assess the ability to follow simple commands or repeat three given words. Memory can then be addressed by asking the patient to recall these words after a few minutes. This approach can help differentiate sleepiness, from a full waking arousal, seizure, or parasomnia.

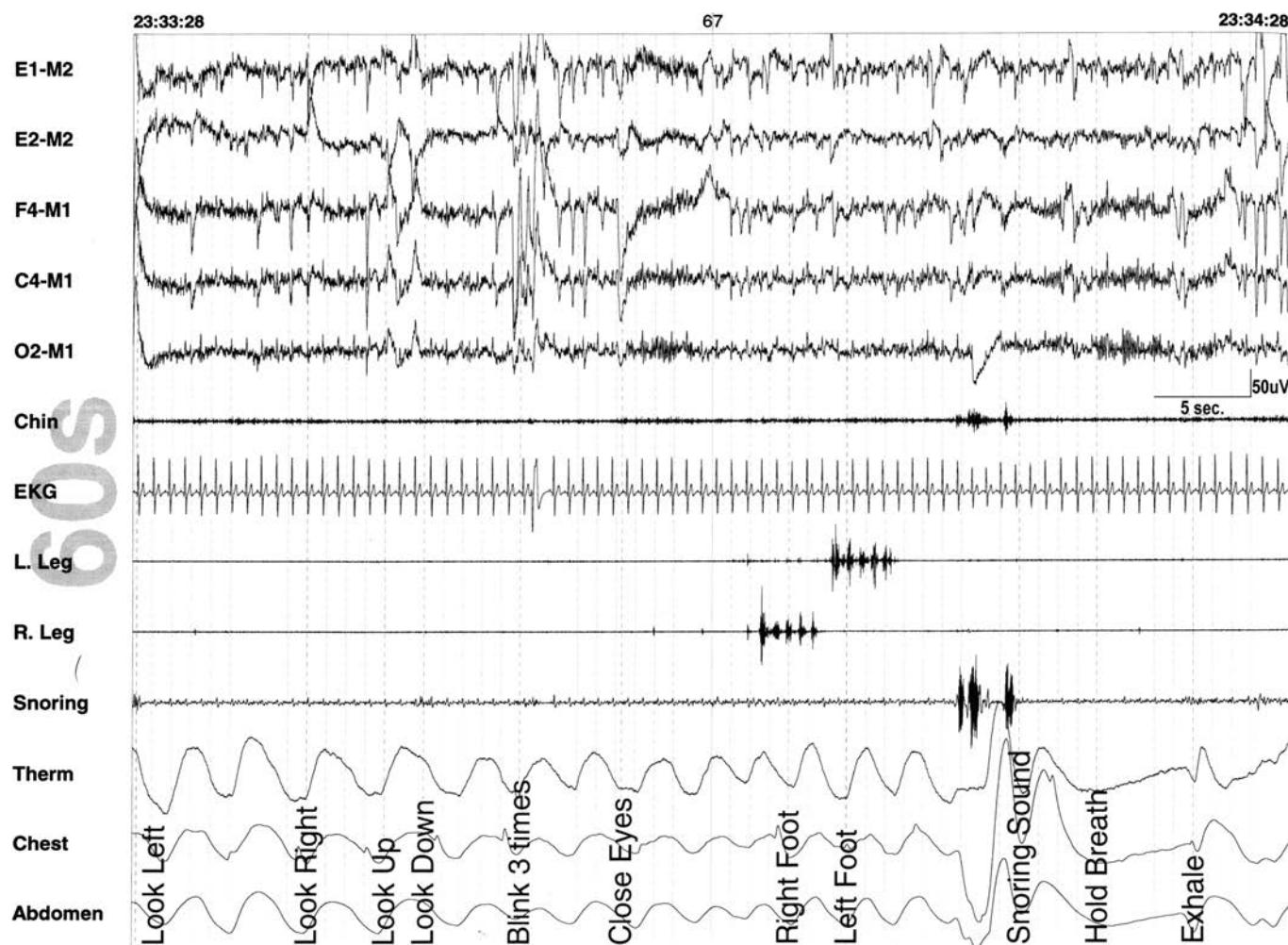
The technologist must document observations on the computer and/or paper. In our laboratory, we require frequent entries (every 15–30 minutes) on our History and Observation form (Fig. 12-11). The table format of this form makes routine entries quick and easy. Observations that must be described and documented include sleep stages, SpO<sub>2</sub> levels, EtCO<sub>2</sub> levels, respiratory events, ECG abnormalities, body position, subjective

snoring level, unusual snoring or breathing sounds, leg or body movements, PAP pressures, response to PAP, bizarre behaviors (including abrupt arousals with vocalizations, parasomnia, or seizure-like activity), bathroom breaks, technologist/patient interaction, and any other observations that may assist with the interpretation of the study. In addition, the History and Observation form should include a final section where the technologist can document their summary of pertinent observations made throughout the night (Fig. 12-12).

### ENDING THE STUDY

The study will end after a minimum of 6 hours of recording (although 8 hours is preferable).<sup>6</sup> "Lights On" time should be documented on the computer and observation form after which physiologic and amplifier calibrations should be performed. The acquisition recording should then be stopped and the data stored according to manufacturer instructions.

The technologist should quietly enter the patient's room, turn on a dim light, and arouse the patient. The patient should be allowed to use the restroom prior to removing electrodes. Electrodes that have been secured with collodion should be carefully removed with acetone or a product specifically designed for collodion removal. Conductive cream or paste should be removed with warm water and any tape should be loosened with an adhesive remover if needed. The patient should then be asked to fill out a post-sleep



**Figure 12-10.** This 60-second epoch demonstrates the physiological calibrations used to verify the integrity of the recording. The technologist ensures that the patient's movement corresponds to the appropriate electrographic signal.

questionnaire that gives their perspective of the night's study. If shower facilities are available, they may now shower and get dressed. Before the patient leaves the laboratory, inform them when and from whom they might expect results of the test. Following a PAP trial, patients should be instructed on where to obtain a PAP machine and what they can expect in regard to follow-up care. Give the patient ample time to ask questions.

## SLEEP STAGE SCORING IN THE NORMAL ADULT POPULATION

The polysomnographic (PSG) criteria for the scoring of wake and sleep stages was originally described by Rechtschaffen and Kales in 1968 in *A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects*.<sup>17</sup> This manual identified Stage W (corresponding to the waking state), Stage NREM (non-rapid eye movement; Stages 1, 2, 3, and 4) and Stage REM (rapid eye movement) sleep and stood as the standard for PSG scoring of wake and sleep over the ensuing 40 years.

In 2004, the AASM formed a steering committee and began the process of developing a comprehensive scoring manual that would update the sleep staging rules as well as address the need for standardization of respiratory, movement, and cardiac event scoring. The *AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*, 1st ed., was published in 2007 and presently serves as the standard reference in regard to electrode derivation and location, recording parameters, and rules for scoring sleep stages, arousals, cardiac events, movement, and respiratory events.<sup>2</sup> The wake/sleep designations now used include Stage W (wakefulness), Stage N1 (NREM 1), Stage N2 (NREM 2), Stage N3 (a combination of NREM 3 and the previously recognized NREM 4 sleep stages), and Stage R (REM).

## SLEEP CYCLES

Sleep cycles were first described by Dement and Kleitman in 1959 after they studied the EEG patterns of 33 subjects over 126 nights.<sup>18</sup> They recognized that following sleep onset the EEG pattern progressed to what is now considered Stage N3 sleep, after which a brief shift back to the lighter stages of NREM sleep occurred before giving way to a REM period (Stage R).

## HISTORY AND OBSERVATION FORM

Name \_\_\_\_\_ Hosp# \_\_\_\_\_ Date \_\_\_\_\_ Age \_\_\_\_\_ DOB \_\_\_\_\_

PSG#\_\_\_\_\_ Computer Drive\_\_\_\_\_ Rm #\_\_\_\_\_ Night #\_\_\_\_\_ Pt. Location\_\_\_\_\_

Referring Dr./Dept. \_\_\_\_\_ Diff. Dx. \_\_\_\_\_

Study Requested: PSG \_\_\_\_\_ MSLT \_\_\_\_\_ CPAP Trial \_\_\_\_\_ BPAP Trial \_\_\_\_\_ Retitration \_\_\_\_\_ Other \_\_\_\_\_

Chart Reviewed by ABSM Diplomate: Signature \_\_\_\_\_ Date \_\_\_\_\_

Medical Hx:

Sleep Hx: (circle)				
Snoring	Frequent arousals	Sleepy driver	Sleep paralysis	Tonsillectomy
EDS	Unrefreshed in a.m.	PLM's	Hypnagogic hallucinations	Adenoideectomy
SOB/gasping	Dry mouth	Act out dreams	Cataplexy	
Morning HA	Weight gain	Sleep walk		

Height:	Previous PSG:
Weight:	Previous EKG:
Neck Circum.	Previous ABG:

**Figure 12-11.** The History and Observation form is a useful tool utilized by the PSG technologist to relay pertinent information to the interpreting physician. This form includes basic patient information, medical and sleep history, and a log of observations.

<b>TECHNOLOGIST'S IMPRESSIONS</b>	
<b>Video Event:</b> _____yes _____no	<b>Other Comments:</b>
<b>Snoring:</b>	
<b>EKG:</b>	
<b>PLMS:</b>	
<b>HOB:</b>	
<b>Supp. O<sub>2</sub>:</b>	
<b>Final Pressure:</b>	
<b>CPAP Mask and Accessories:</b>	
<b>Mask:</b> Type/Brand _____	
Nasal _____ Full-Face _____ Total Face _____	
SM _____ MD _____ LG _____ Other _____	
<b>Headgear:</b> Simple Strap _____ Other _____	
<b>Chin Strap:</b> Regular _____ Deluxe _____ N/A _____	
<b>Humidity:</b> Cool _____ Heated _____ N/A _____	
<b>Pt. educated regarding HHC setup and given "Where To Go From Here" form _____</b>	
<b>Technologist Signature:</b>	

**Figure 12-12.** On the final page of our laboratory's History and Observation form, there is a space designated "Technologist's Impression" where a succinct summary of the final recording parameters can be provided. In addition, a "Comments Section" allows for a more detailed narrative in regard to the technologist's overall impression of the study.

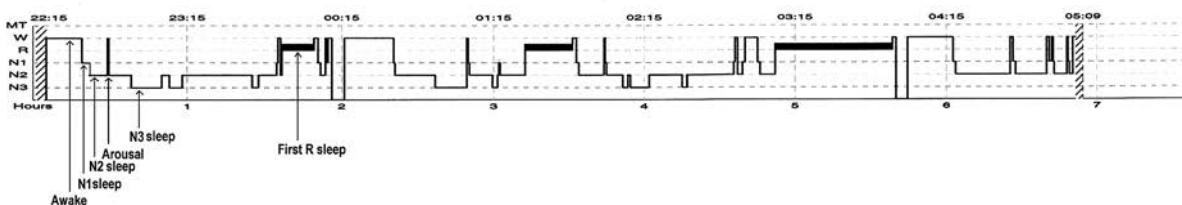
They found that this cyclical pattern repeated itself every 90 to 100 minutes throughout the night.

As the night progresses, during the typical sleep of a young adult, the REM periods become more prolonged, Stage N3 becomes shorter, and N2 increases to occupy the majority of the NREM cycles. Sleep stage percentages in a normal young adult are as follows: Stage W = <5%; Stage N1 = 2% to 5%; Stage N2 = 45% to 55%; Stage N3 = 13% to 23%; Stage REM = 20% to 25%.<sup>19</sup> Once the sleep stage data is compiled at the end of a

study, the histogram is generated and provides a concise snapshot of the sleep cycles (Fig. 12-13).

### SCORING

The recommended EEG derivation necessary to facilitate the scoring of sleep stages is recorded from the frontal, central, and occipital regions (F4, C4, O2)<sup>2</sup> as many sleep-related electroencephalographic phenomena tend to arise from these areas. For



**Figure 12-13.** Once sleep stage scoring is complete, the histogram (or hypnogram) is generated automatically. This is a visual tool that in a single glance provides an immediate and concise overview of the patient's sleep architecture.

scoring purposes, the recording is divided into 30-second segments that are formally referred to as “epochs”. A specific wake/sleep stage is assigned to each epoch beginning at “lights out” using the new nomenclature that includes stages W, N1, N2, N3, and R. It should be mentioned that although most acquisition systems have a computer-assisted scoring function, the AASM mandates that recordings scored using this function be reviewed for accuracy and edited as needed. In our experience, manual scoring by a trained technologist provides a greater level of consistency and accuracy.

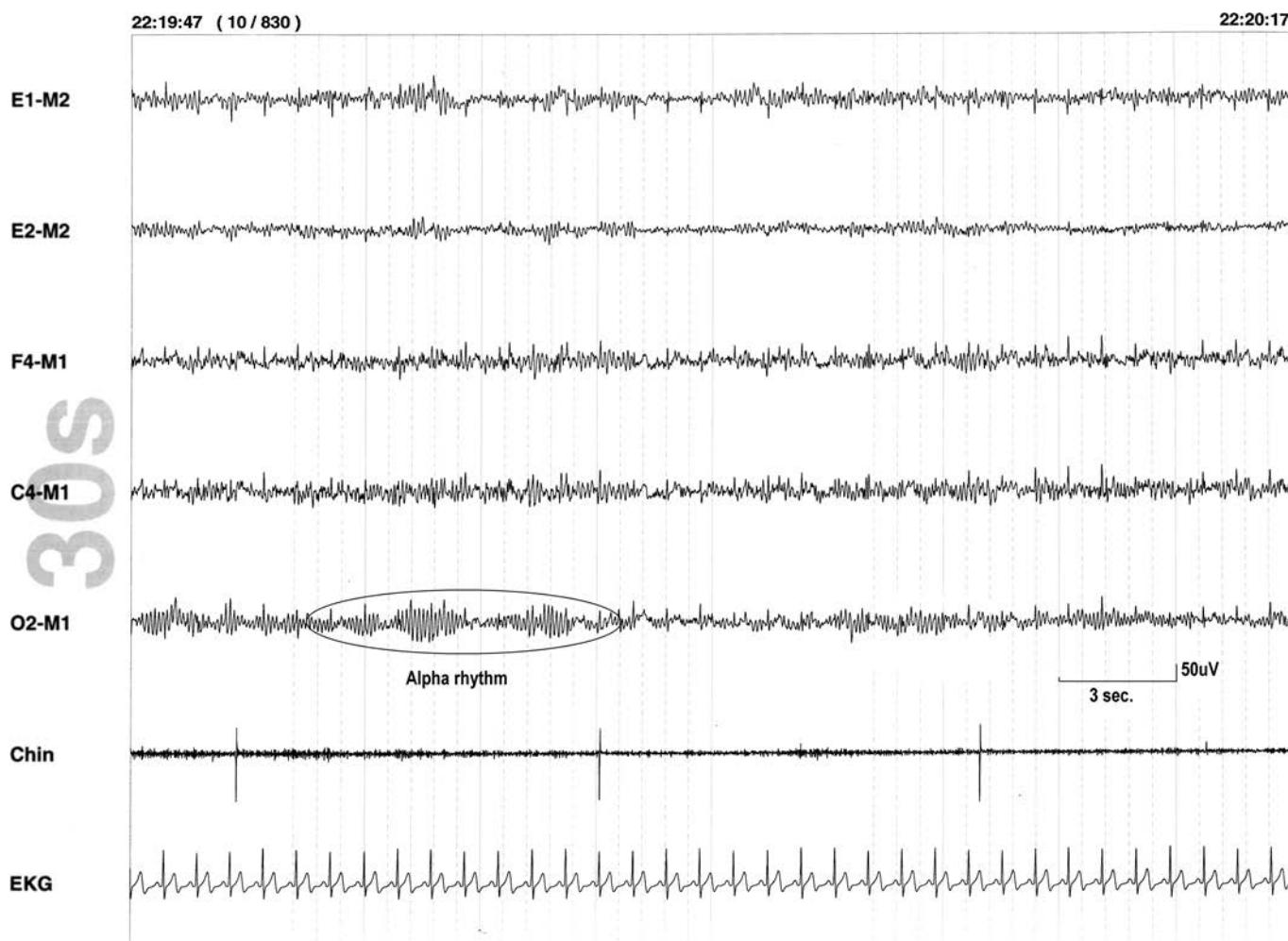
### Stage W (Wakefulness)

Stage W corresponds to the waking state and is scored as such when alpha rhythm in the occipital area is present in greater than 50% of the epoch (Fig. 12-14).<sup>2</sup> Alpha rhythm is described as 8 to 13-Hz activity most prominent in the posterior region that is enhanced upon eye closure and relative mental inactivity.<sup>20</sup> The rhythm is attenuated when the patient opens their eyes or during periods of active cognitive processing (calculating etc.). Epochs where alpha is attenuated but eye blinks or conjugate eye movements and normal or high chin muscle activity continue, will be scored as W. Close clinical observation and carefully addressing eye blinks and elevated muscle activity is

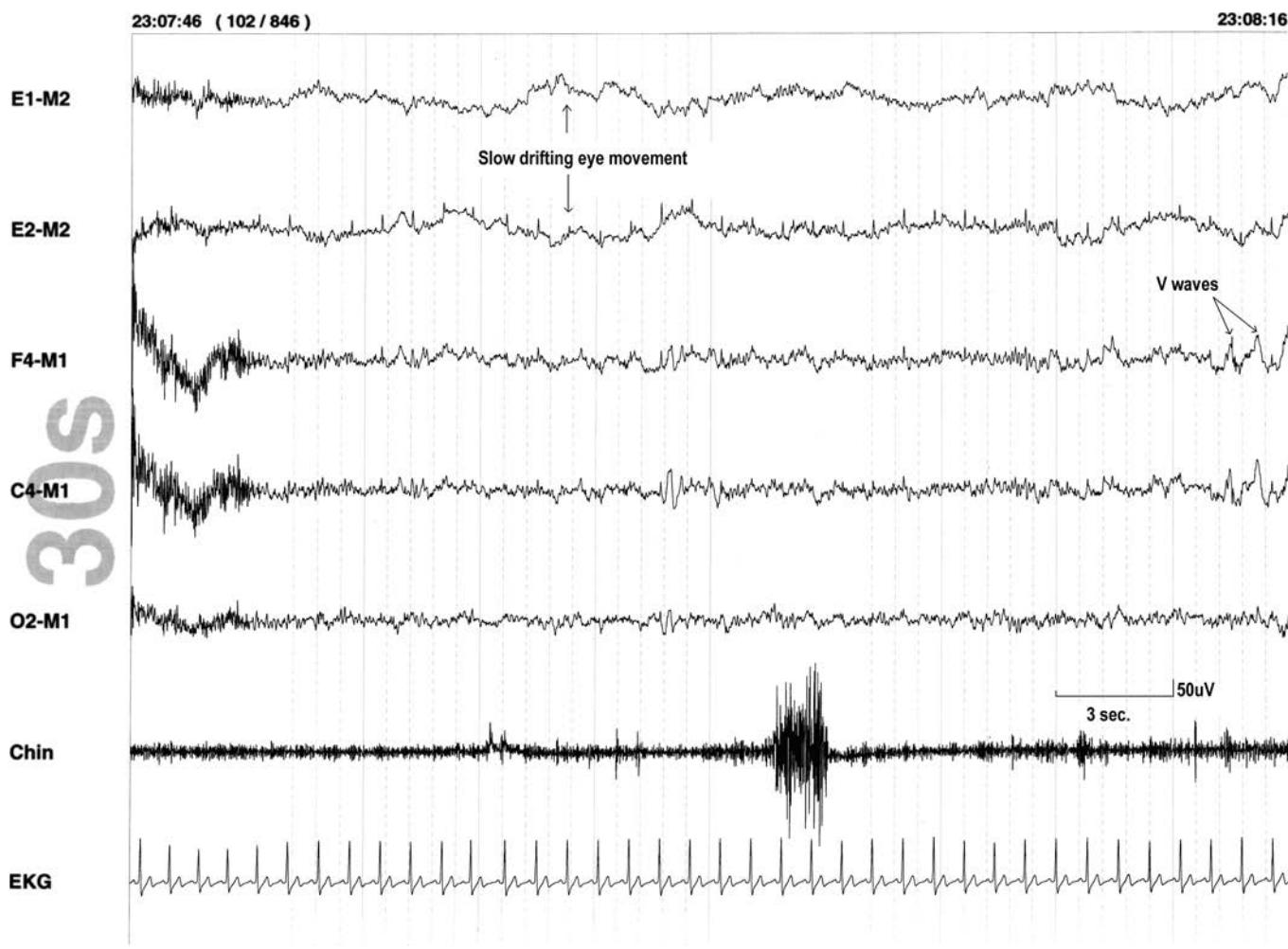
important as approximately 10% of the normal population does not have a measurable alpha activity, and up to one third have alpha activity that is widely distributed (see pages 103–115 in *Practical Guide: EEG* for further detail).<sup>21</sup>

### Stage N1

Scoring of stage N1 sleep (drowsiness) begins when alpha activity is replaced by a slower low-amplitude, mixed-frequency rhythm that persists for greater than 50% of an epoch (Fig. 12-15).<sup>2</sup> If the patient did not have a distinct alpha rhythm during Stage W from which to make a comparison, then N1 should be scored as soon as any of the following occur: vertex sharp waves (V waves), slow eye movements (SEMs), or theta activity with a slowing of the waking background frequency by  $\geq 1$  Hz. SEMs are described as slow drifting conjugate, horizontal eye movements, with a sinusoidal morphology. It is important to note that although V waves and SEMs are often present during stage N1, they are not required to score N1. The chin muscle may vary during stage N1 but tends to be lower than stage W. Positive occipital sharp transients of sleep (POSTS) are also seen in stage N1. POSTS are recognized in the occipital leads as down-going in referential recording or surface positive sharp transient discharges that are usually less than 50  $\mu$ V in amplitude.<sup>22</sup>



**Figure 12-14.** This example of stage W demonstrates alpha activity (most prominent in the occipital channel) occupying greater than 50% of the epoch.



**Figure 12-15.** An example of N1: Alpha rhythm has been replaced by low-amplitude mixed-frequency activity with increased theta and V waves at the frontal and central electrodes in greater than 50% of this epoch. Slow drifting eye movements are noted as well, with absence of K-complexes and spindles.

### Stage N2

There is a progressive increase in background theta wave activity with more distinctive V waves and POSTS in stage N2 sleep. Nevertheless, scoring stage N2 requires the presence of, and is classically characterized by sleep spindles and/or K-complexes.<sup>2</sup> Initially, the appearance of sleep spindles in the frontal and central regions defines the onset of stage N2 sleep. Sleep spindles are rhythmic trains of 11 to 16 Hz fusiform waves with an amplitude generally less than 50  $\mu$ V and a duration of greater than or equal to 0.5 seconds, which occur periodically throughout N2 sleep typically in runs lasting 1 to 2 seconds. The K-complex is described as a high-amplitude, frontally dominant, delta-theta sharp wave burst frequently appearing as a surface negative sharp wave followed by a positive wave with a duration of at least 0.5 seconds.<sup>23</sup> A K-complex can occur spontaneously or occur as part of an arousal phenomena following external stimulation. This paroxysmal type waveform stands out from the background activity, which helps distinguish it from slow waves found in stage N3 sleep. Sleep spindles often are superimposed on or follow a K-complex.

*Onset of Stage N2:* N2 is scored when one or more runs of sleep spindles or K-complexes (unassociated with arousals)

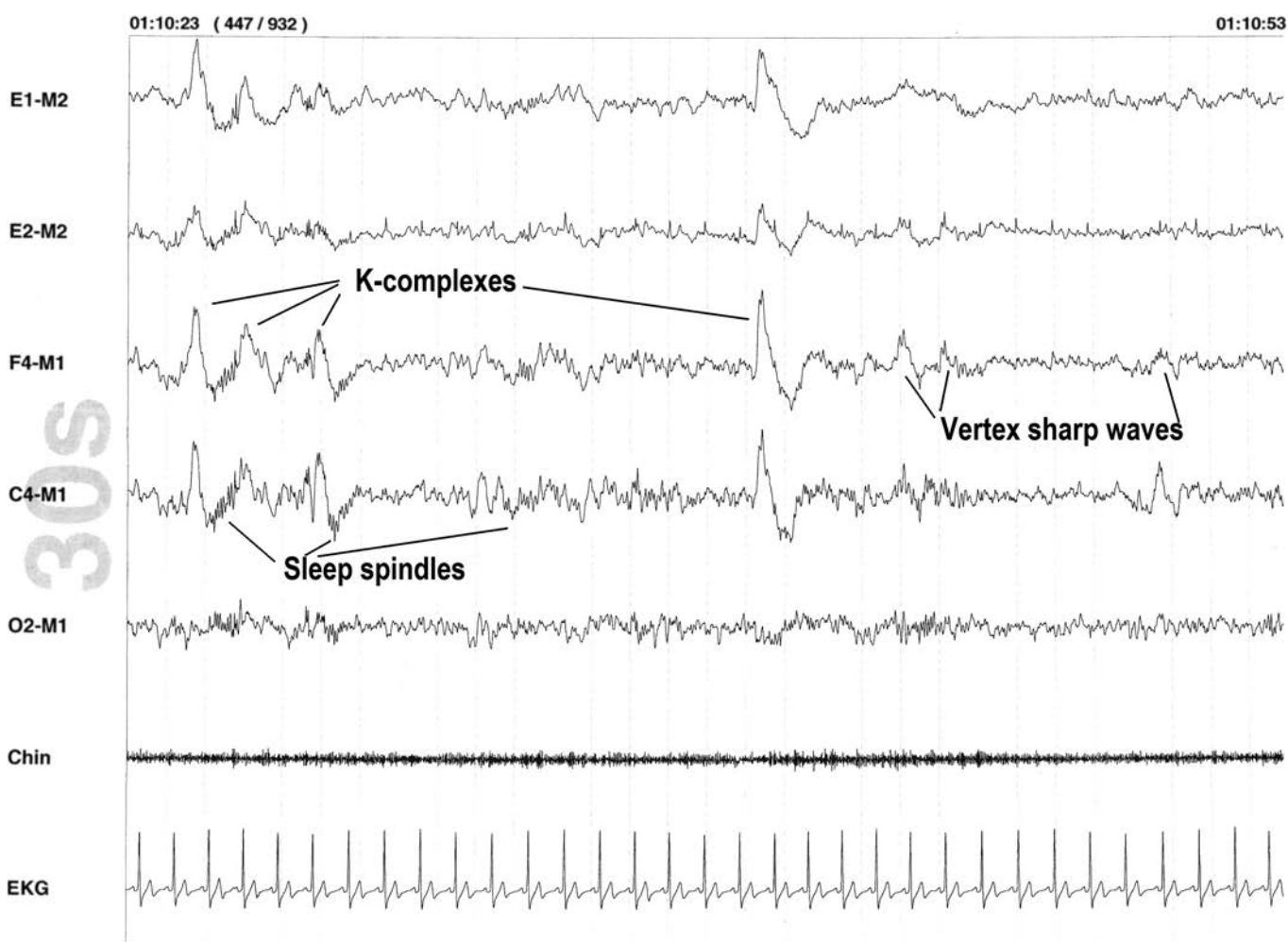
occurs either during the first half of an epoch or the last half of the previous epoch (Fig. 12-16).

*Continuation of Stage N2:* Epochs with low-amplitude, mixed-frequency activity with a paucity of K-complexes and sleep spindles should continue to be scored as N2 if the preceding epoch displays either sleep spindles or K-complexes (without arousal).<sup>2</sup>

*End of Stage N2:* Stage N2 ends when the following occurs: there is a clear transition to stage W, N3 or R; transition to N1 if an arousal occurs followed by a paucity of K complexes and sleep spindles.

### Stage N3

Stage N3 sleep, previously known as “slow wave” or “delta sleep,” is most prominent in the first third of the night. Stage N3 sleep is scored when 20% or more of an epoch is occupied by the classically defined high-amplitude slow-wave activity with a frequency of 0.5 to 2 Hz and peak-to-peak amplitude of greater than 75  $\mu$ V (Fig. 12-17).<sup>2</sup> The chin EMG is variable and often very low. Sleep spindles and K-complexes can continue into stage N3 sleep; however, sleep spindles are generally slower in frequency and more frontally dominant. Conversely, the REMs



**Figure 12-16.** An example of stage N2: K-complexes and sleep spindles in the first half of this epoch along with the absence of slow wave activity indicates the onset of stage N2.

classically associated with wakefulness and stage R sleep are typically absent during stage N3 sleep.

#### Stage R Sleep

REM sleep, sometimes referred to as “paradoxical or dream sleep,” is classically reported to occur approximately 90 to 120 minutes after sleep onset, with the duration of each REM period becoming longer as the night progresses, and as such with the greatest percentage of stage R sleep occurring in the final third of the night. Periods of stage R sleep are associated with autonomic instability as evidenced by a relative poikilothermia (absence of internal temperature control) and an irregularity in the heart rate, blood pressure, and respiratory rate.<sup>24-26</sup>

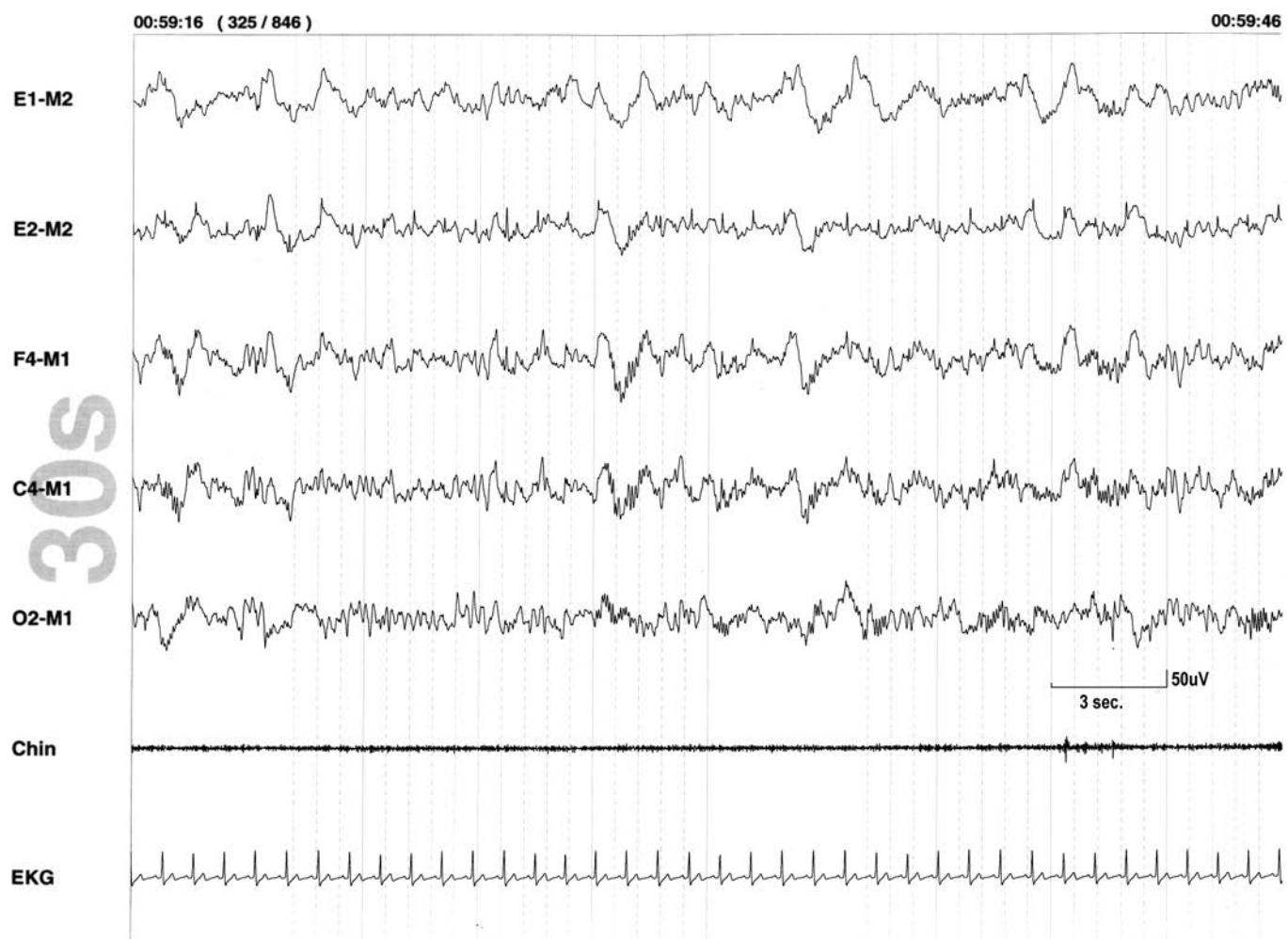
Common EEG features found in REM sleep are rapid eye movements (REMs), a low-amplitude mixed-frequency brain wave pattern, low chin EMG, sawtooth waveforms, and a general overall atonia (tonic REM) with intermittent episodes of transiently elevated paroxysms of muscle activity (phasic REM). The transient muscle activity of phasic REM is recognized as short bursts (typically <0.25 seconds) of elevated activity noted most prominently in the chin and anterior tibialis EMG channels

that tends to occur during REMs (Fig. 12-18). REMs captured in the EOG channels are appreciated as irregular and sharp conjugate eye movements (see Fig. 12-18). Sawtooth waveforms are trains of sharply contoured 2 to 6 Hz waves (with a “saw-like” appearance) that may appear maximally over the central regions of the brain (see Fig. 12-18).

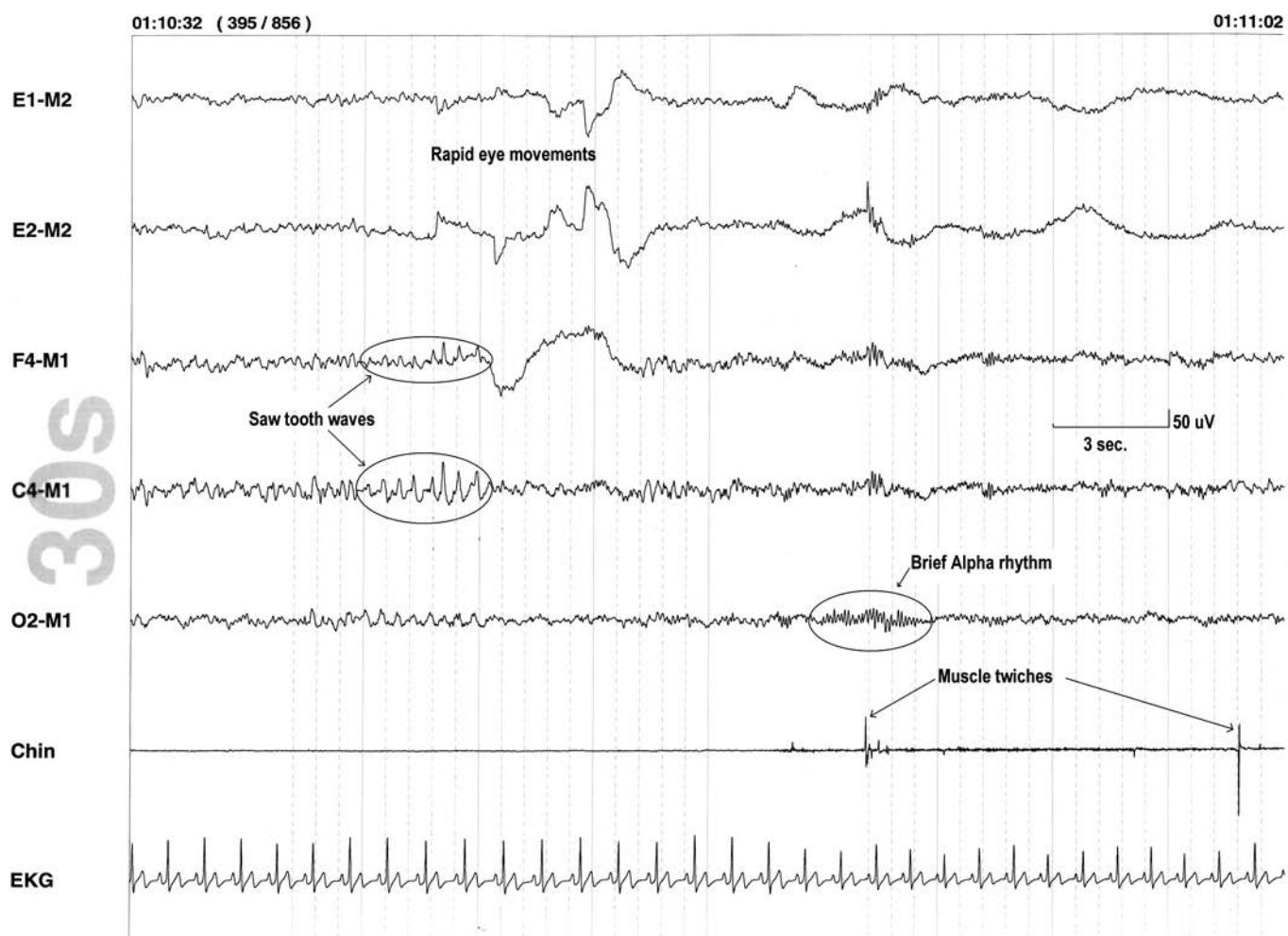
*Onset of Stage R:* The following three features must be present for an epoch to be scored as stage R sleep: a low-amplitude, mixed-frequency EEG pattern; low or absent chin activity (commonly the lowest amplitude of the night); REMs (Fig. 12-19).<sup>2</sup>

*Continuation of Stage R:* After REM onset has been clearly defined, if an individual epoch has a paucity of REMs, continue to score stage R as long as there is an absence of sleep spindles and K-complexes and the EEG continues to demonstrate a low-voltage, mixed-frequency background along with chin EMG atonia (Fig. 12-20).<sup>2</sup>

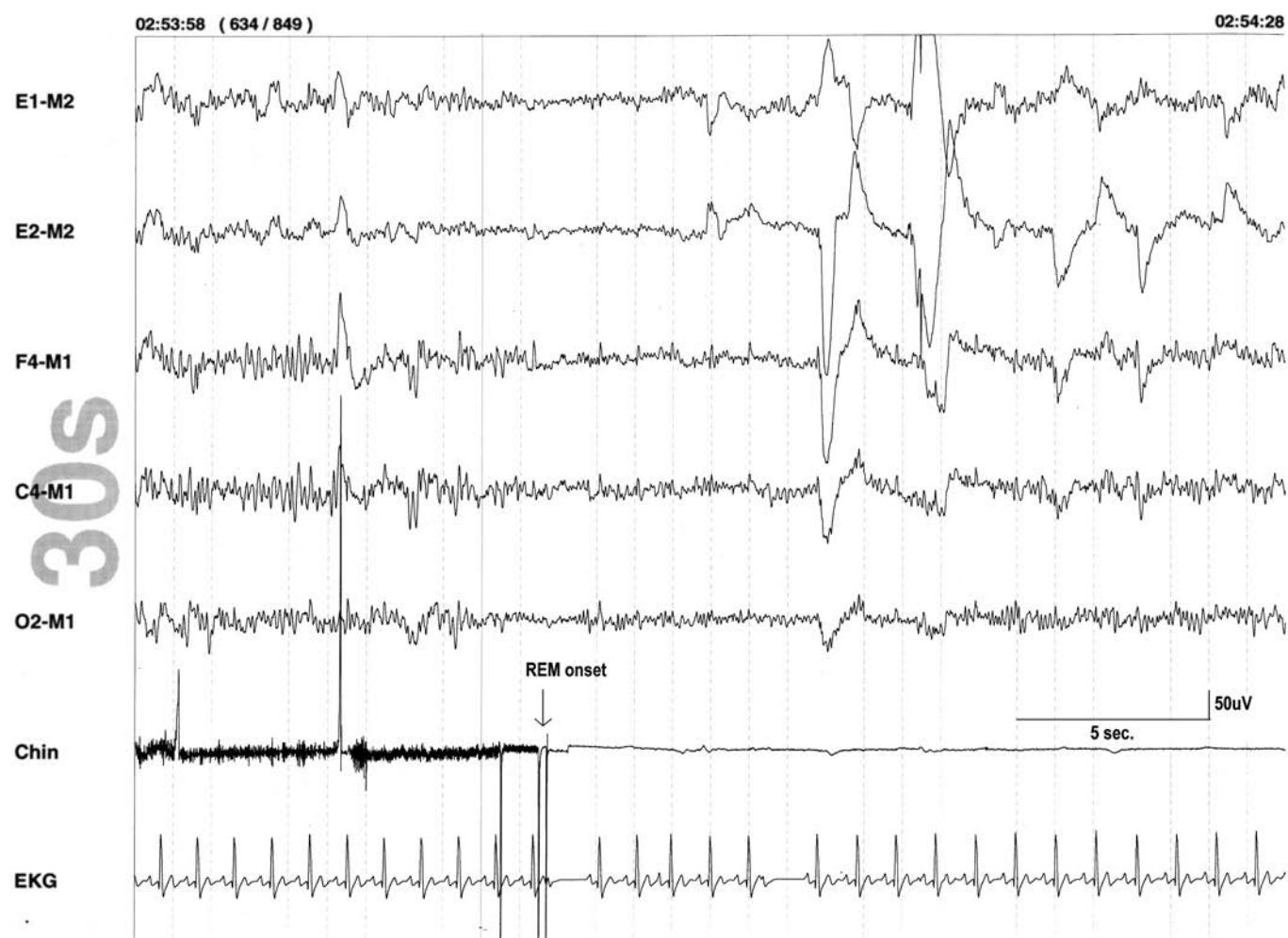
*End of Stage R:* Stage R ends if one of the following occurs: a transition to stage W or N3 sleep; chin EMG increases or an arousal occurs followed by the scoring criteria that defines stage N1; a K-complex or sleep spindle appears in the first half of an epoch without REMs (even if the chin EMG remains low) (Fig. 12-21).<sup>2</sup>



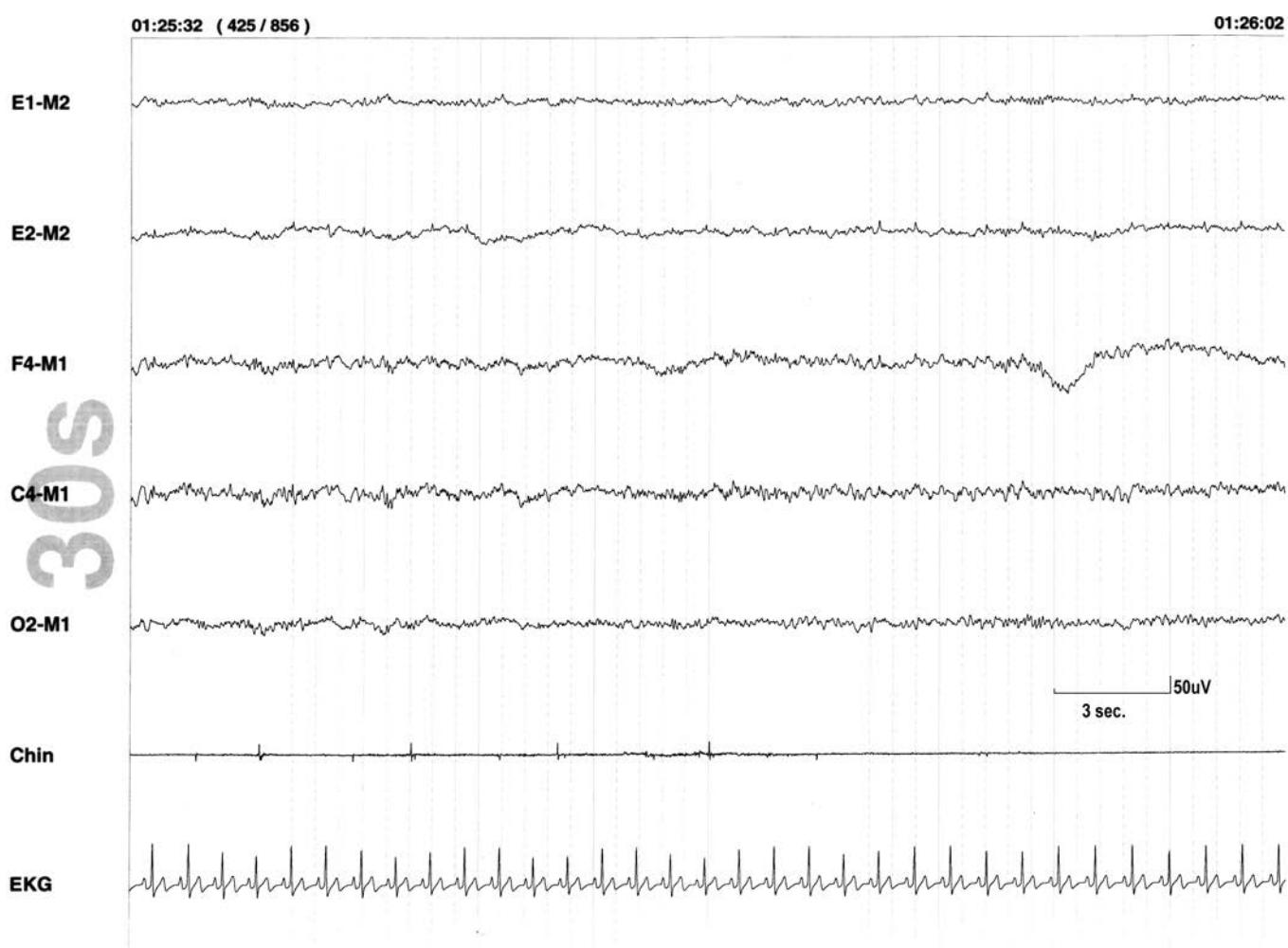
**Figure 12-17.** An example of stage N3: Over 20% of this epoch of stage N3 is occupied by high-amplitude slow-wave activity.



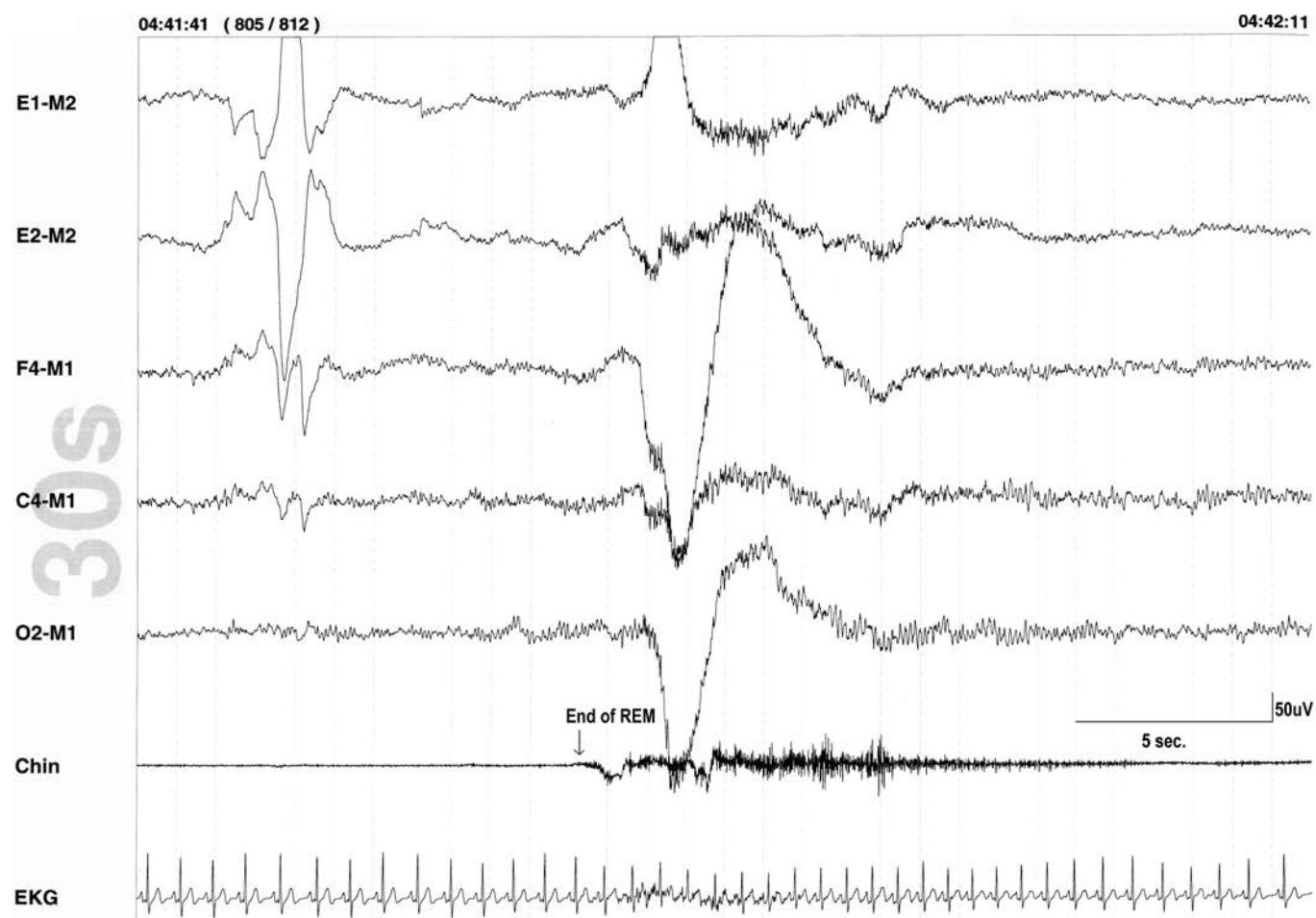
**Figure 12-18.** An example of stage R sleep: There are REMs, sawtooth waveforms, low chin EMG, muscle twitches, and low-voltage mixed-frequency activity with brief intrusion of alpha rhythm. The presence of REMs and muscle twitches indicate that this is phasic REM sleep



**Figure 12-19.** An example of onset of stage R: REM sleep begins 10.5 seconds into the epoch as the chin EMG activity abruptly drops out and the fast-frequency background activity is replaced by a low-amplitude mixed-frequency EEG pattern along with REMs.



**Figure 12-20.** An example of a continuation of stage R sleep: This epoch was preceded by stage R, and despite the absence of REMs, there continues to be low chin EMG and a low-amplitude mixed-frequency pattern in the absence of spindles and K-complexes.



**Figure 12-21.** An example of end of stage R: This epoch has an arousal with an increase in chin EMG and a return of the alpha rhythm indicating a shift to stage W.

<b>TABLE 12.4</b>	<b>AASM's Recommended Sleep Staging and Movement Event Parameters, Definitions, and Formulas to be Reported in the Sleep Report</b>	
<i>Parameter</i>	<i>Definition</i>	<i>Formula</i>
<b>SLEEP STAGING</b>		
Lights Out (clock time)	Official beginning of the study.	
Lights On (clock time)	Official end of the study.	
Total Sleep Time (TST)	Total time in minutes spent asleep.	
Total Recording Time (TRT)		TRT – TWT OR total time of stage N1 + N2 + N3 + R
Sleep Latency (SL)	Total time in minutes from lights out to lights on.	(Lights On epoch – Lights Out epoch) ÷ 2
Stage R Latency	Time in minutes from lights out to sleep onset.	(Sleep Onset epoch – Lights Out epoch) ÷ 2
Wake After Sleep Onset (WASO)	Time in minutes from Sleep Onset to REM Onset.	(REM onset epoch – Sleep Onset epoch) ÷ 2
Sleep Efficiency (SE)	Total time spent awake after first epoch of sleep.	TRT – TST – SL
Time in each stage of sleep	Total percentage of recording time spent asleep.	(TST ÷ TRT) × 100 (%)
Percentage of TST in each stage	Time in minutes spent in each stage of sleep.	(Time in each stage ÷ TST) × 100 (%)
<b>MOVEMENT EVENTS</b>		
PLMS	Total number of periodic limb movements in sleep.	
PLMS w/arousal	Total number of periodic limb movements in sleep associated with arousals.	
PLMS index	Number of periodic limb movements per hour of sleep.	(PLMS ÷ TST) × 60
PLMS arousal index	Number of periodic limb movements associated with arousals per hour of sleep.	(PLMS w/arousal ÷ TST) × 60

### **Major Body Movements**

A body movement is defined as a movement causing muscle artifact that obscures the EEG for more than half an epoch and makes the recording indiscernible. Epochs containing body movements are scored as follows: score as stage W if any alpha rhythm is present; if the epoch is either preceded or followed by an epoch of stage W, score as stage W; if neither of the previous criteria apply, score the epoch the same as the epoch following the body movement.<sup>2</sup>

### **REPORT**

Once the sleep study is completed and the technologist has scored the study, a report is generated to assist the physician with the interpretation. These reports can be designed to fit the needs of each individual lab. Although most acquisition systems can be programmed to generate a report automatically, it is advantageous for the technologists and physicians to understand the formulas used to create the data to ensure the accuracy of the report. Table 12.4 shows the AASM's recommended sleep scoring and movement event data that are to be incorporated into the polysomnography report.

### **SCORING OF PERIODIC LIMB MOVEMENTS IN SLEEP (PLMS)**

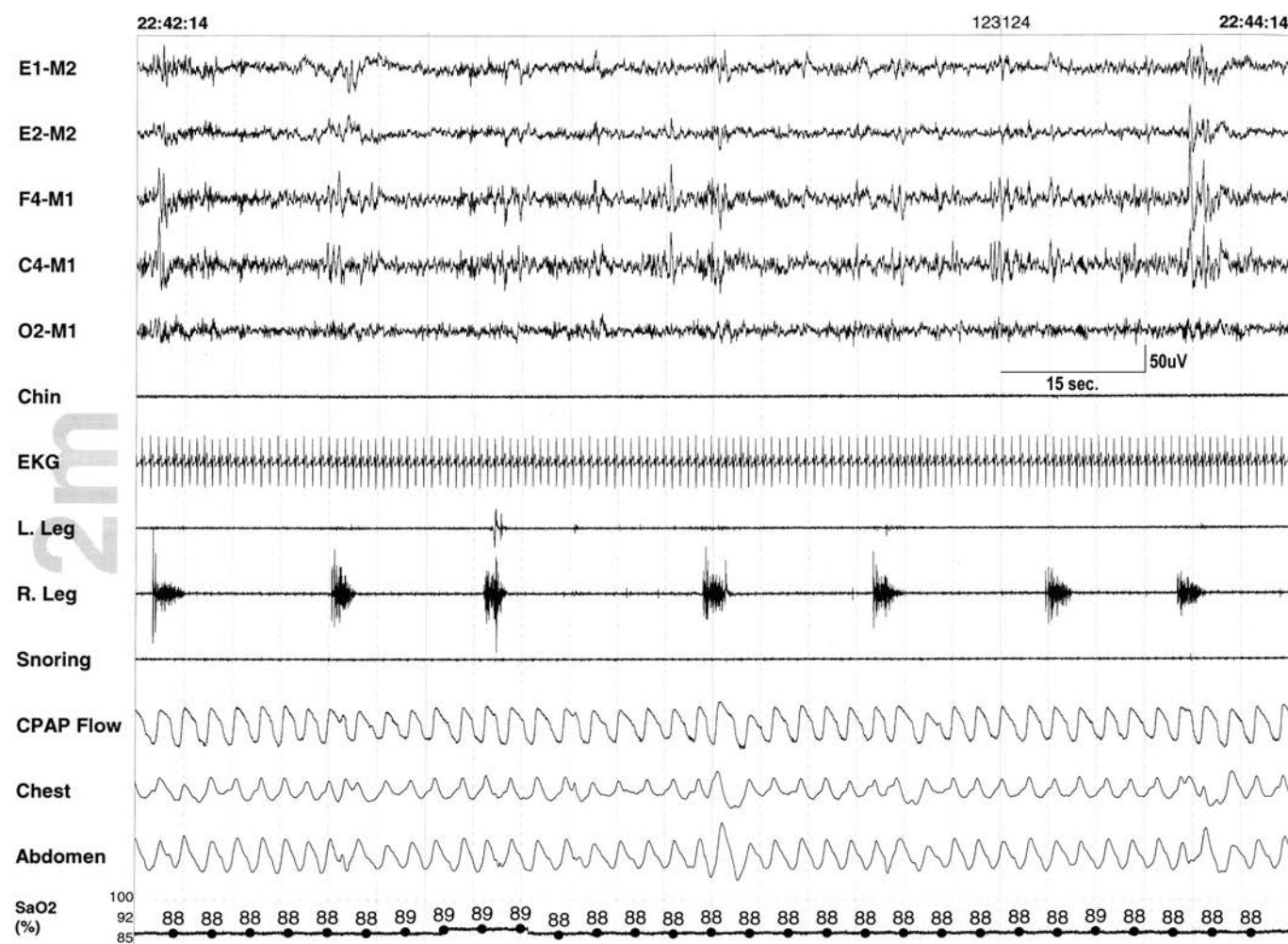
Periodic limb movements in sleep (PLMS) are generally described as periodic, repetitive, and stereotypical limb movements that typically involve extension of the big toe, and at times can even involve flexion of the ankle, knee, and hip.<sup>27</sup> PLMS are most prevalent during the first half of the night in stage N2

sleep. While many patients are unaware of these movements, their sleep may be disrupted, leaving them with complaints of daytime sleepiness. Although PLMS are fairly common and occur in up to 34% of people over the age of 60 years, they are also classically reported in up to 90% of patients with restless leg syndrome, 65% of narcoleptics, and 70% of individuals diagnosed with REM sleep behavior disorder.<sup>27</sup>

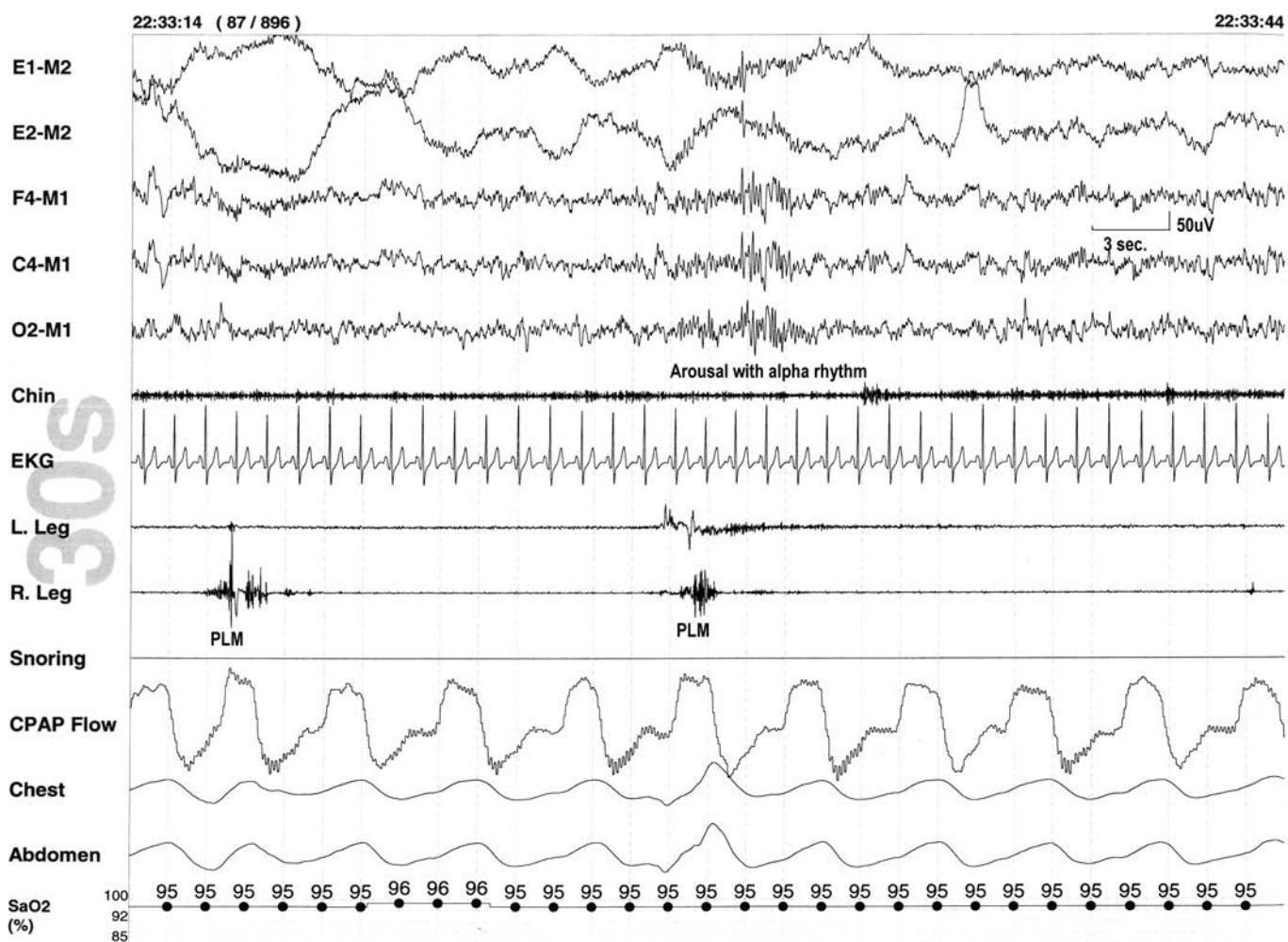
A single leg movement (LM) event is scored when the LM shows a minimum amplitude increase of 8 µV above the resting EMG baseline and the duration of that LM lasts from 0.5 to 10 seconds. The duration of a single LM is measured from the point where the EMG amplitude has increased by 8 µV above the resting baseline, to the point where the EMG amplitude subsequently drops to a level ≤ 2 µV above the resting baseline. When LMs occur in separate leg channels, they are counted as a single event if their onsets occur within 5 seconds of each other. To be considered a PLM series, there must be a minimum of four consecutive LMs with an interval between events (measured from onset to onset) ranging from 5 to 90 seconds (Fig. 12-22).<sup>2</sup>

In addition, each individual leg movement must be formally scored as occurring either "with" or "without" an arousal. A PLM "with" arousal event should be scored when there is a time span of less than 0.5 seconds between the movement and an associated arousal (regardless of which comes first). An arousal is defined as an abrupt shift in EEG frequency that includes alpha, theta, and beta frequencies (excluding sleep spindles) and lasts ≥ 3 seconds. The arousal must also follow 10 seconds of established sleep (Figs. 12-23 and 12-24).<sup>2</sup>

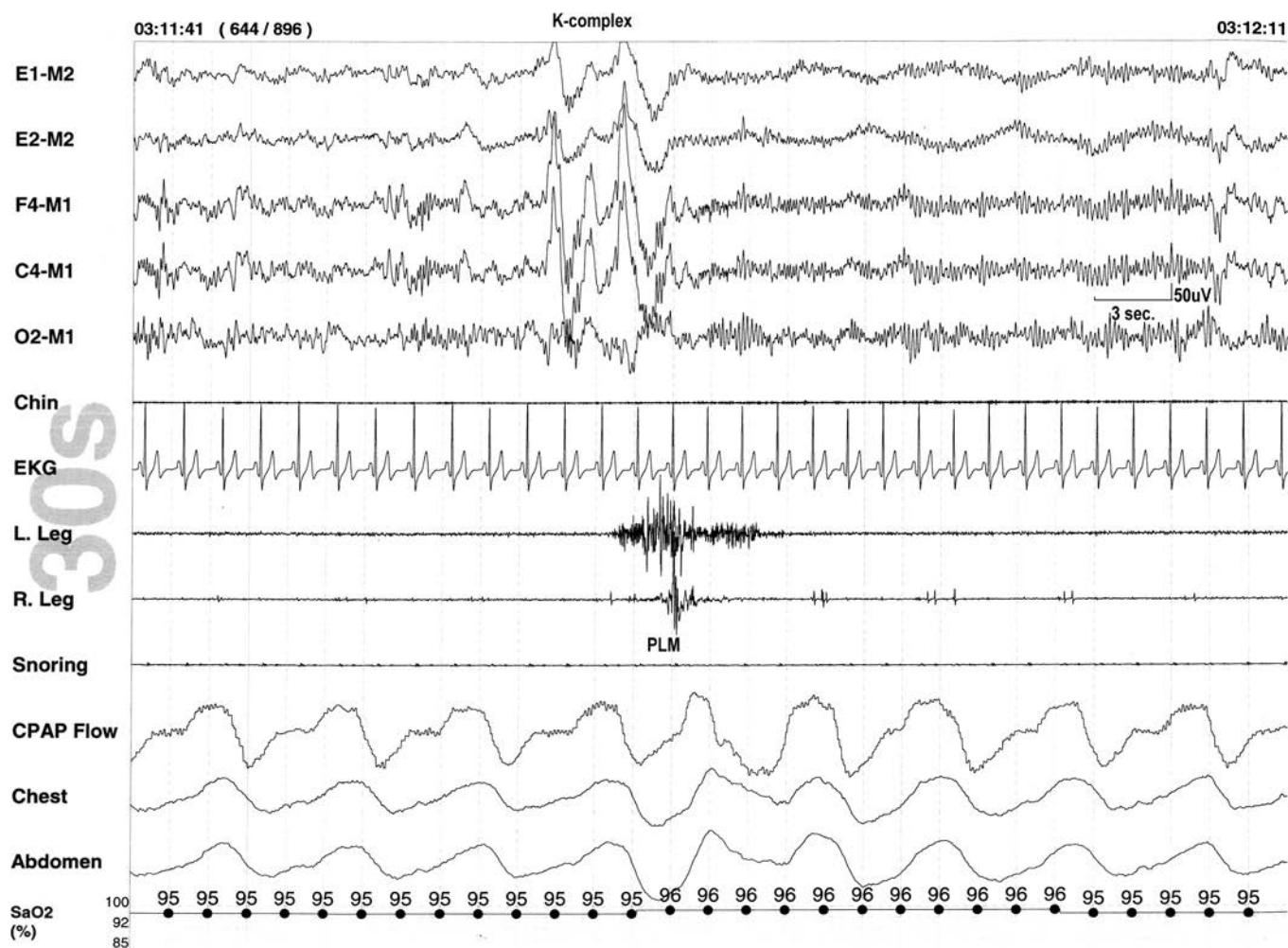
Finally, a limb movement occurring 0.5 seconds prior to or following an apneic/hypopneic event should not be scored when determining PLMS. In this situation, the limb movement is probably an artifact resulting from an underlying sleep related breathing disorder.



**Figure 12-22.** These periodic leg movements occurring every 15 to 20 seconds represent a PLMS series. As the PLM could occur in either the left or the right limb, it is important to record from both legs. No arousal response was associated with the PLMs in this epoch.



**Figure 12-23.** The second PLM during N2 sleep is associated with a brief EEG arousal.



**Figure 12-24.** This example shows a periodic leg movement preceded by K-complex arousal.

## SUMMARY

The study of sleep disorders is regarded as a branch of medicine in its infancy. The accurate diagnosis of most health-related problems is heavily dependent on a complete history. Nevertheless, intrinsic to most sleep disorders is a relative paucity of history as the patient is often asleep during the pathology of interest. To some extent, the advent of the PSG has allowed us to overcome this problem. As such, the performance of a high-quality PSG by a well-trained technologist has proven to be of great value in the diagnosis and treatment of sleep-related breathing problems, disorders of excessive sleepiness, parasomnias, seizures, and a variety of movement disorders in sleep.

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# Sleep Apnea and Related Conditions

## INTRODUCTION

One of the most prevalent sleep disorders and therefore one of the most thoroughly researched aspects of sleep medicine is sleep apnea. There are millions of individuals who exhibit the signs and symptoms of sleep apnea that are undiagnosed and subsequently untreated. What may be deemed as benign snoring or a restless night may actually be indicative of a more insidious pathology. Additionally, there are several related conditions that fall under the rubric of sleep disordered breathing that ultimately affect the sleep and breathing architecture of these individuals. Generally, the decision to refer a patient to a sleep center is based on the desire to discern and diagnose treatable sleep disordered breathing. Therefore, it is through the increased awareness and suspicion of both clinicians and patients that sleep apnea can be properly managed.

The aim of this chapter is to highlight the methods by which a diagnosis of sleep apnea and related conditions is made and, through a discussion of the various treatment modalities and pathophysiology, create a familiar if not applicable understanding of this ubiquitous sleep disorder.

## EPIDEMIOLOGY

Quite often, the term *sleep apnea* is used interchangeably with *sleep-disordered breathing* or more specifically *obstructive sleep apnea* (OSA). The goal is to describe a disorder in which sleep is complicated by pauses in an individual's breathing cycle that may be in the setting of increased respiratory effort. The number of individuals who are actually affected by sleep apnea is the greatest concern.

It is projected that 26% of adults are at a significant risk of developing OSA and the prevalence of OSA when defined as an apnea/hypopnea index of greater than five events per hour is approximately 20%.<sup>1</sup> It is also estimated that 85% to 90% of individuals affected by sleep apnea are undiagnosed and untreated.<sup>2</sup> However, a conservative estimate of the prevalence of undiagnosed OSA in western countries is approximately 5%.

The prevalence of OSA increases from 18 to 45 years of age, with two- to threefold higher prevalence in those who are over the age of 65 compared to those who are between 30 and 64 years old.<sup>3</sup> Interestingly, OSA is seemingly more prevalent in African American men and women who are under 35 years of age compared to Caucasians of the same age group.<sup>5</sup> Some

studies suggest that OSA is more common in men than women.

There are many risk factors that predispose individuals to OSA including obesity or being overweight, tobacco use, heredity, diabetes, and those with large neck sizes or narrow upper airway.<sup>5</sup> Medications that can lead to a decrease in upper airway muscle activity include benzodiazepines, narcotics, and alcohol. Additional risks are delineated in Table 13.1.

## DEFINITION OF SLEEP APNEA

### SLEEP-RELATED BREATHING DISORDERS

Sleep-related breathing disorders are characterized by impaired ventilation during sleep in the setting of abnormal respiratory patterns. These respiratory patterns include apneas, hypopneas, respiratory effort-related arousals (RERAs), or hypventilation. Clinically, these patterns may be difficult to distinguish from one another despite a thorough history and witnessed events. Polysomnography provides an objective method in which to document and differentiate each pattern based on selective criteria. There are four types of sleep-related breathing disorders<sup>12</sup>:

- Obstructive sleep apnea/Hypopnea syndromes
- Central apnea syndrome
- Hypoventilation/hypoxemia syndromes associated with sleep
- Undefined/nonspecific sleep disorders

### OBSTRUCTIVE SLEEP APNEA AND HYPOPNEA

OSA is defined as an absence of airflow in the setting of continued ventilatory effort (Fig. 13-1). Scoring of such an event must meet the criteria for apnea and demonstrate increased and/or continued respiratory effort throughout the duration of the absence of airflow. This is precipitated by nearly complete, or total upper airway obstruction.

Many patients with OSA have a reduced cross-sectional airway diameter that may be due to a significantly compliant airway or an excessive amount of soft tissue. It is thought that the collapsibility of the upper airway ultimately affects the degree of ventilatory instability.<sup>4</sup> During sleep, there is an involuntary mechanism that causes hypotonia of the pharyngeal musculature. The combination of a relaxed pharyngeal musculature and smaller airway can cause an absence or a reduction

**TABLE 13.1****Risk Factors for OSA**

Overweight (BMI of 25–29.9) and Obese (BMI > 30) individuals
Family members with OSA
Smokers
Ethnic minorities
Middle aged men, older men, postmenopausal women
Individuals with large neck sizes: Men >17 inches, women >16 inches
Diabetes
Craniofacial/upper airway soft tissue abnormalities
Nasal Congestion
Narrow upper airway

in airflow, which is termed *apnea* or *hypopnea*, respectively. The body attempts to overcome this, increasing the respiratory drive, leading to inspiration and therefore a re-establishment of airflow. The  $\text{SaO}_2$  desaturation associated with apnea/hypopnea usually occurs 15 to 20 seconds after the resumption of respiration.

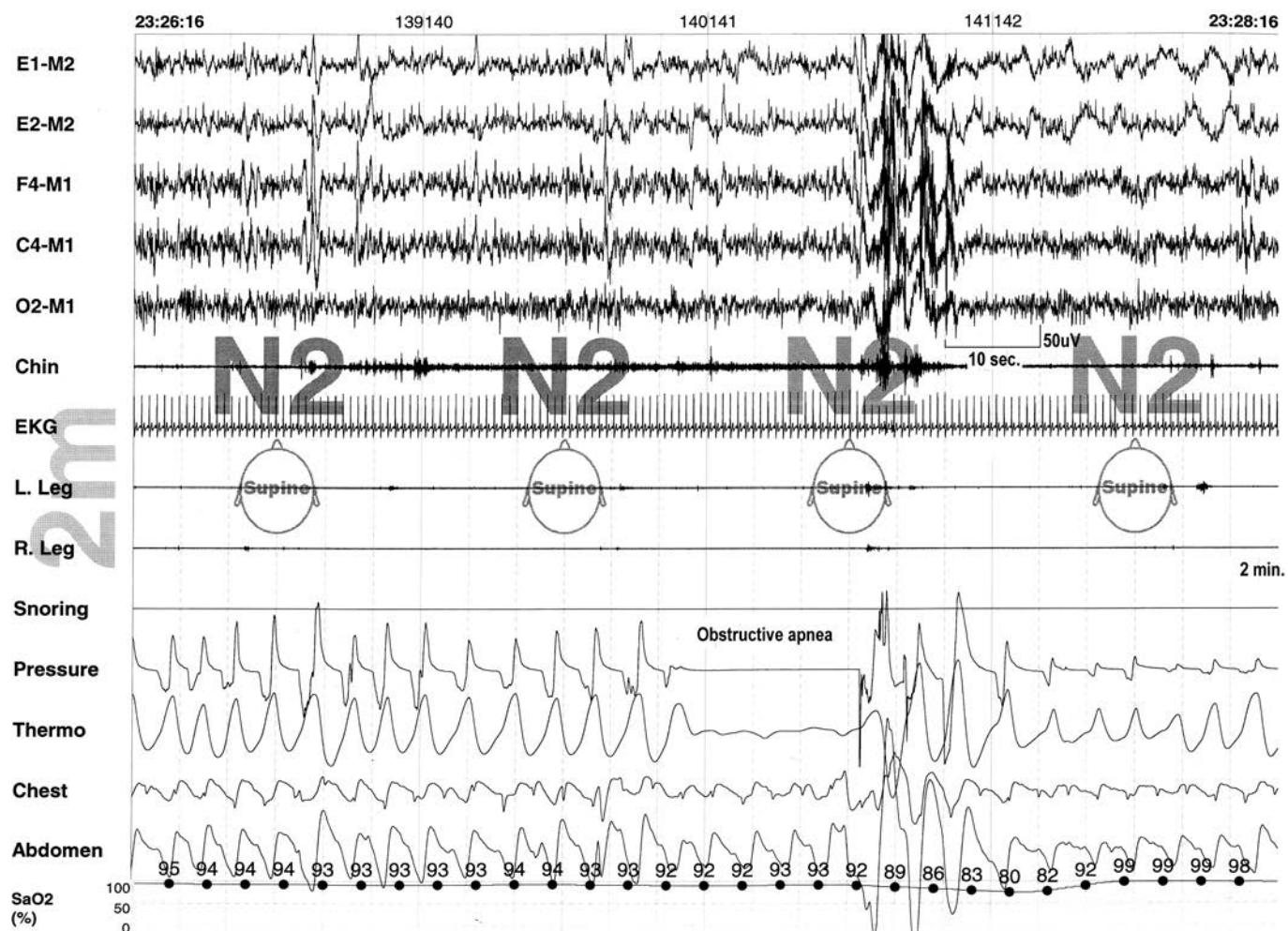
As mentioned above, apnea is defined as the absence or near absence of airflow. The most recent American Association of Sleep Medicine (AASM) Manual for the Scoring of Sleep and

Associated Events uses the following criteria to score the polysomnogram in patients suspected of having sleep disordered breathing.<sup>6</sup> An apnea can be defined when the following criteria are met:

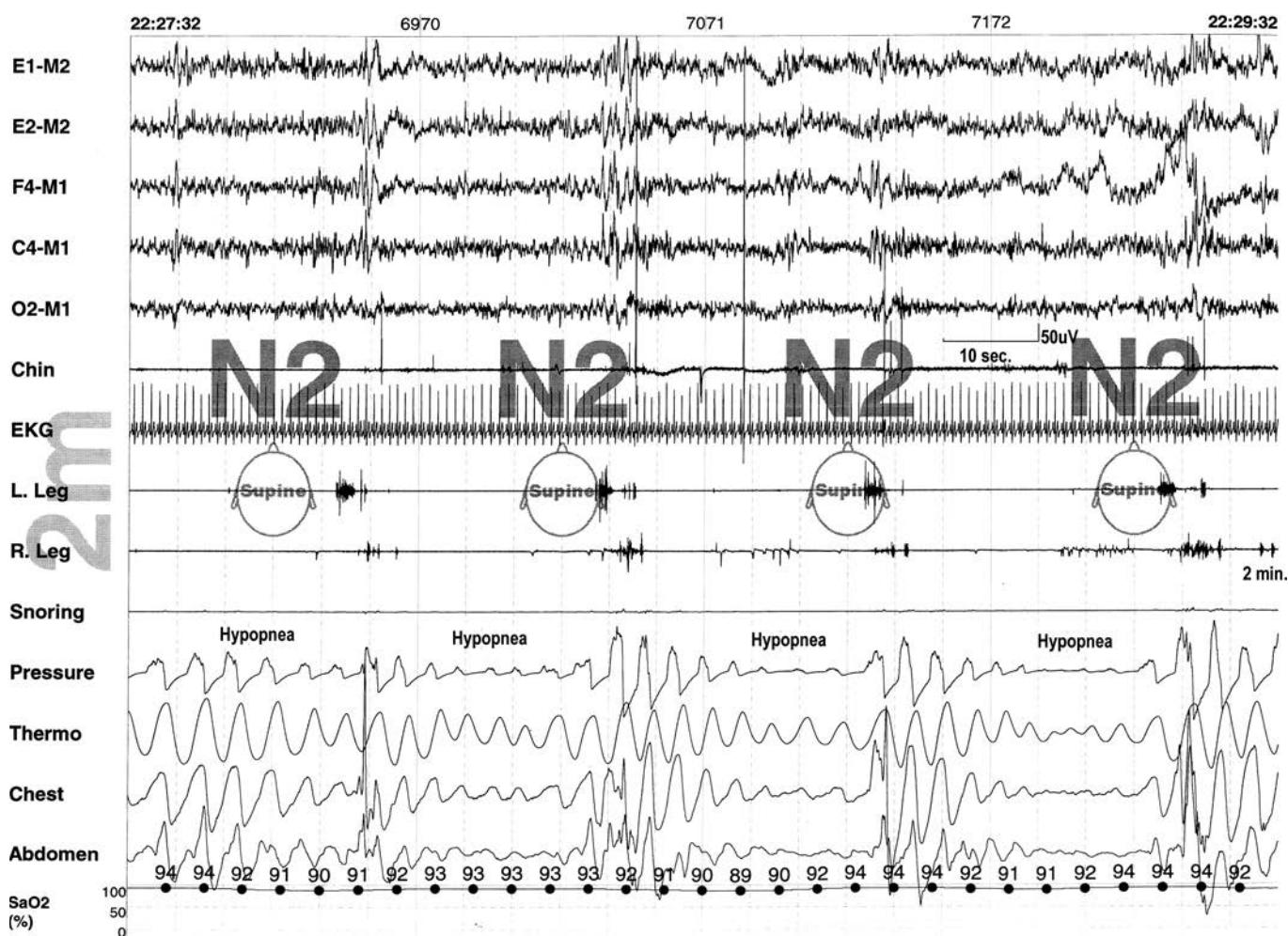
- Peak thermal sensor excursion must demonstrate a decrement of greater than or equal to 90% of the baseline, lasting greater than or equal to 10 seconds.
- Greater than or equal to 90% of the event meets the above amplitude reduction criteria.
- An oxygen desaturation is not required to score an apnea.

Hypopnea (Fig. 13-2) is defined as a reduction in airflow that does not meet the criteria for apnea. The hypopnea scoring criteria are as follows:

- There is a decrement of airflow lasting greater than or equal to 10 seconds.
- There is at least a 4% desaturation from baseline (pre-event).
- There is at least a 30% reduction in the nasal pressure signal reading from the baseline.
- Of the diminished airflow, greater than or equal to 90% of the event must meet the criteria of amplitude reduction ( $\geq 30\%$ ) from the baseline.



**Figure 13-1.** An obstructive apnea showing an  $\text{SaO}_2$  desaturation down to 80% (baseline  $\text{SaO}_2$  93%–94%) after 17 seconds of apnea. The lowest  $\text{SaO}_2$  desaturation occurred at about 20 seconds after the resumption of respiration. Note no air flow measured by nasal pressure sensor and minimal excursion by thermal sensor (>90% reduction), while maintaining chest and abdominal movements. Note the lowest  $\text{SaO}_2$  desaturation.



**Figure 13-2.** Four episodes of hypopnea during 2 minutes of N2 sleep showing an  $\text{SaO}_2$  desaturation to 89% to 91% from a baseline of 94%. Note a significant decrease of the nasal pressure sensor (>50% reduction) with each hypopnea. Also note the burst of fast EEG activity at the end of each event, indicating a brief arousal.

An alternative scoring criterion for hypopnea is as follows:

- There is a decrement of airflow lasting at least 10 seconds.
- There is at least a 3% desaturation from the baseline (pre-event) or if event is associated with an arousal.
- There is at least a 50% reduction in the nasal pressure signal from the baseline.

It should be noted that there are healthy individuals who may have periods of reduced or absent respiration during normal sleep, especially during sleep onset or REM (rapid eye movement) sleep. Again, these episodes would not meet the aforementioned criteria nor necessarily have the associated symptoms of sleep apnea.

Many patients have both apnea and hypopnea (Fig. 13-3). When describing the severity of OSA, therefore, the combined number of apneas and hypopneas (AH index [AHI]) is commonly used. The AHI refers to the number of apneas and hypopneas per hour of sleep. Based on this value, OSA can be defined as mild, moderate, or severe (Table 13.2).

Patients with the designation of Mild OSA usually have an AHI between 5 to 15 events per hour. Associated symptoms can be sedentary daytime sleepiness that does not impair one's daily activity. These tend not to be recognized by the patient. Nevertheless, the

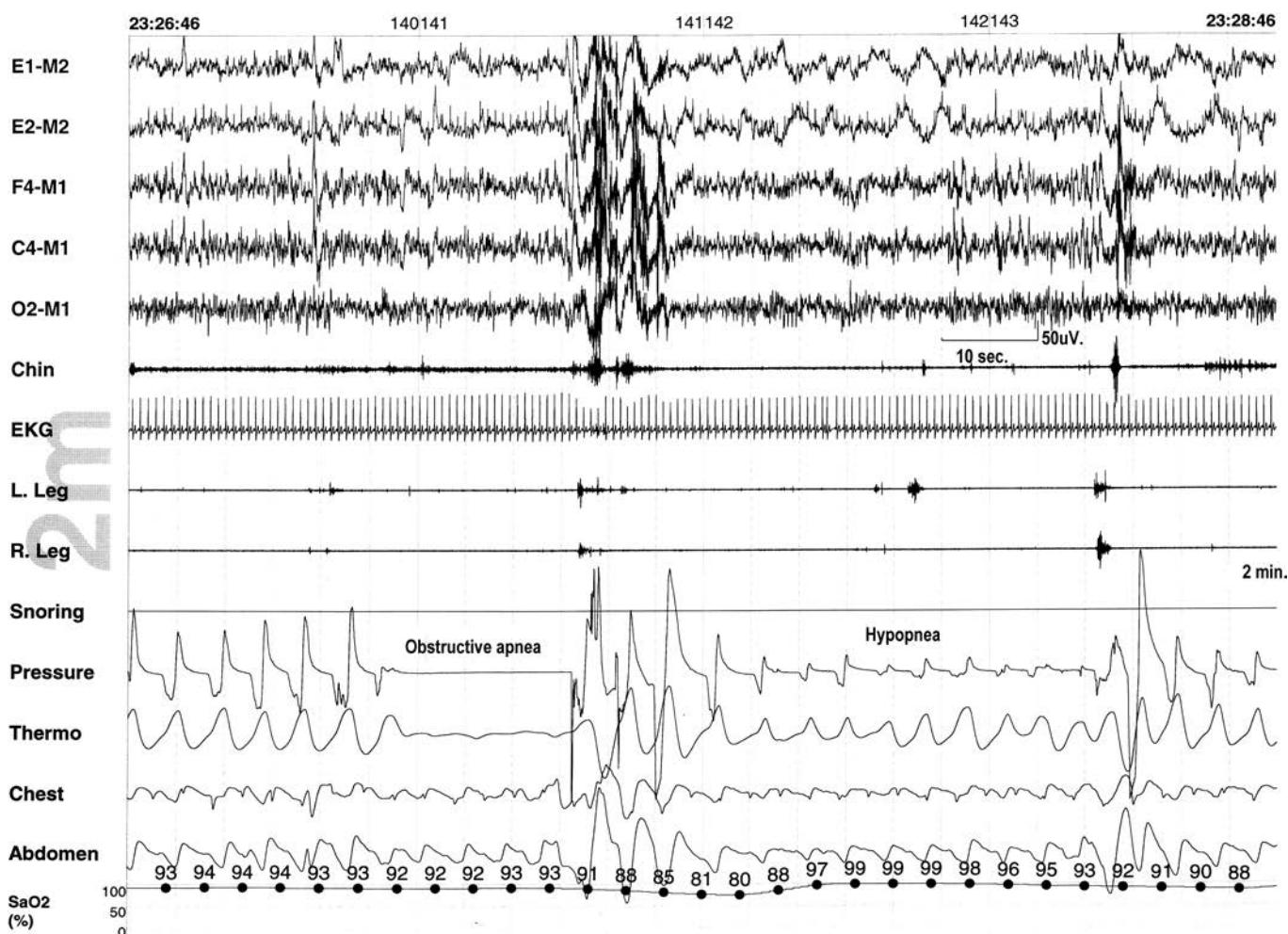
patient may be able to discern a difference in the quality of life after treatment (i.e., behavior modification, abstinence from alcohol, or positive airway pressure [PAP] therapy) is instituted.

Moderate OSA is defined as an AHI between 15 and 30. These patients tend to be aware of their daytime sleepiness and have altered their lifestyle to preclude falling asleep at inappropriate times. Unfortunately, individuals with moderate OSA can have an increased incidence of having motor vehicle accidents among an increased rate of associated comorbidities.<sup>7</sup>

Finally, severe OSA is defined as an AHI of greater than 30 events per hour. The daytime sleepiness experienced impairs normal daily activities and these individuals are at risk for accidental injury when they fall asleep inappropriately. Additionally, many patients with severe OSA can have concomitant comorbidities related to their sleep pathology.

#### CENTRAL APNEA

Central apnea is defined as both the absence of ventilatory effort and airflow (Fig. 13-4). Scoring of such an event has to meet the criteria of apnea and demonstrate a cessation of inspiratory effort despite the absence of airflow. Diaphragmatic inactivation is usually the etiology for such a breathing pattern. A predominance of central apneas during a polysomnogram



**Figure 13-3.** An example of an obstructive apnea lasting 20 seconds and a hypopnea lasting 45 seconds during 2 minutes of N2 sleep. Both events are associated with oxygen desaturation and EEG arousal.

suggests central sleep apnea (CSA) syndrome, a type of sleep-related breathing disorder. This can be idiopathic (also known as *primary*) or secondary, which can be caused by heart failure, stroke, or induced by certain medications.

#### OTHER APNEAS

A mixed apnea is scored when the initial portion of the event demonstrates an absence of inspiratory effort, while the remainder of the event shows a recommencement of the inspiratory effort (Fig. 13-5). Again, the duration of the event should still meet the criteria for apnea as previously described.

A RERA does not meet the criteria for hypopnea or apnea; however, it demonstrates increased respiratory effort or flattening of the nasal pressure waveform that occurs for at least 10 seconds, ultimately leading to an arousal from sleep.<sup>6</sup>

**TABLE 13.2** Classification of OSA Severity

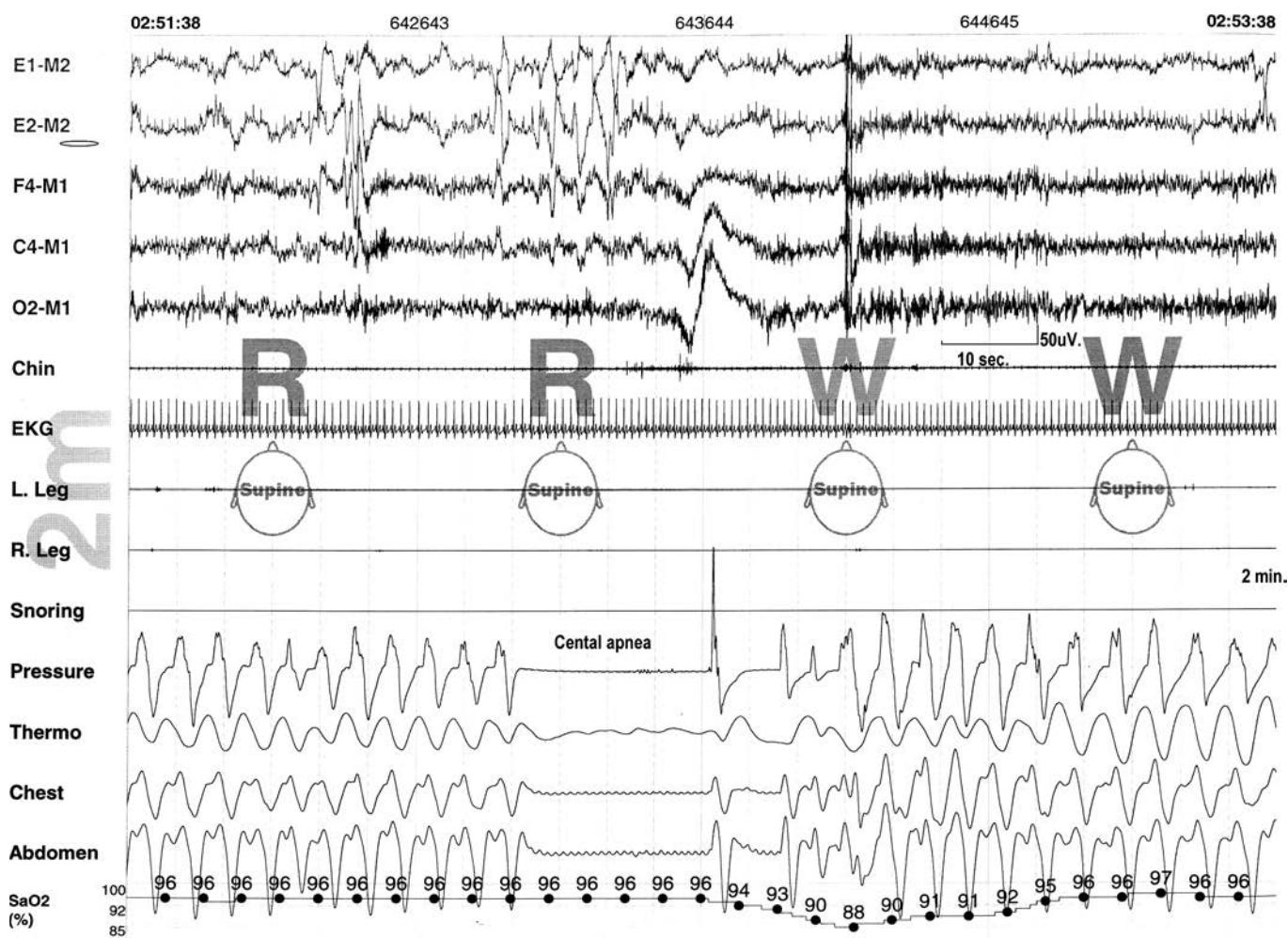
Mild OSA: AHI of 5–15
Moderate OSA: AHI of 15–30
Severe OSA: AHI of >30

#### CLINICAL FEATURES

One of the most common complaints that patients with sleep apnea, and usually their annoyed bed partners, describe is snoring. Many times, this is brought to the attention of a health care provider and in the correct clinical setting can lead to the suspicion of sleep apnea. Snoring is a fairly common phenomenon that occurs during sleep and may increase with age. However, studies have shown that patients with an AHI of less than 5 and who snore loudly each night, are seven times more likely to develop OSA. Snoring is not pathognomonic for sleep apnea, however, in the correct clinical setting should lead to further investigation.

Daytime sleepiness is another component of OSA that many may mistakenly attribute to other events, behaviors, or medical concerns. Patients initially describe fatigue or a general desire to sleep for most of the day. Further inquiry usually uncovers difficulty staying awake in sedentary situations like watching television, reading, or even driving. The Epworth Sleepiness Scale is a screening tool that helps to quantify how sleepy an individual is throughout the day.

Bed partners are encouraged to assist in the initial evaluation of snoring and daytime sleepiness given that many patients



**Figure 13-4.** A central apnea lasting 20 seconds during REM sleep with an  $\text{SaO}_2$  desaturation down to 88% from baseline of 96%. Note the absence of inspiratory effort as well as airflow. The event was terminated by movement and an awake EEG pattern with resumption of respiration.

may be unaware of how frequent their symptoms are or how significant the effects are on their daily activities.

Table 13.3 presents symptoms that can also be present in patients with suspected OSA.

## POLYSOMNOGRAPHIC FEATURES OF SLEEP APNEA

Typically, there are two types of studies that employ polysomnography for the diagnostic evaluation of OSA. The first is a full-night study, in which a patient is solely monitored for the duration of a set number of hours, usually overnight. Based on these findings, the patient may be brought back for a subsequent study where PAP is instituted and titrated as needed to improve the overall sleep architecture and mitigate apnea spells.

A split night study is similar; however, testing and treatment is completed over the duration of a single night. The first part of the study is purely diagnostic while the second portion is actually used to titrate PAP. This is done when the patient shows a significant amount of respiratory events and the diagnosis of sleep apnea is definitive during the first portion of the recording.

As mentioned previously, there are established scoring criteria used by sleep technologists and sleep specialists that

facilitate the recognition of sleep apnea and other related conditions.

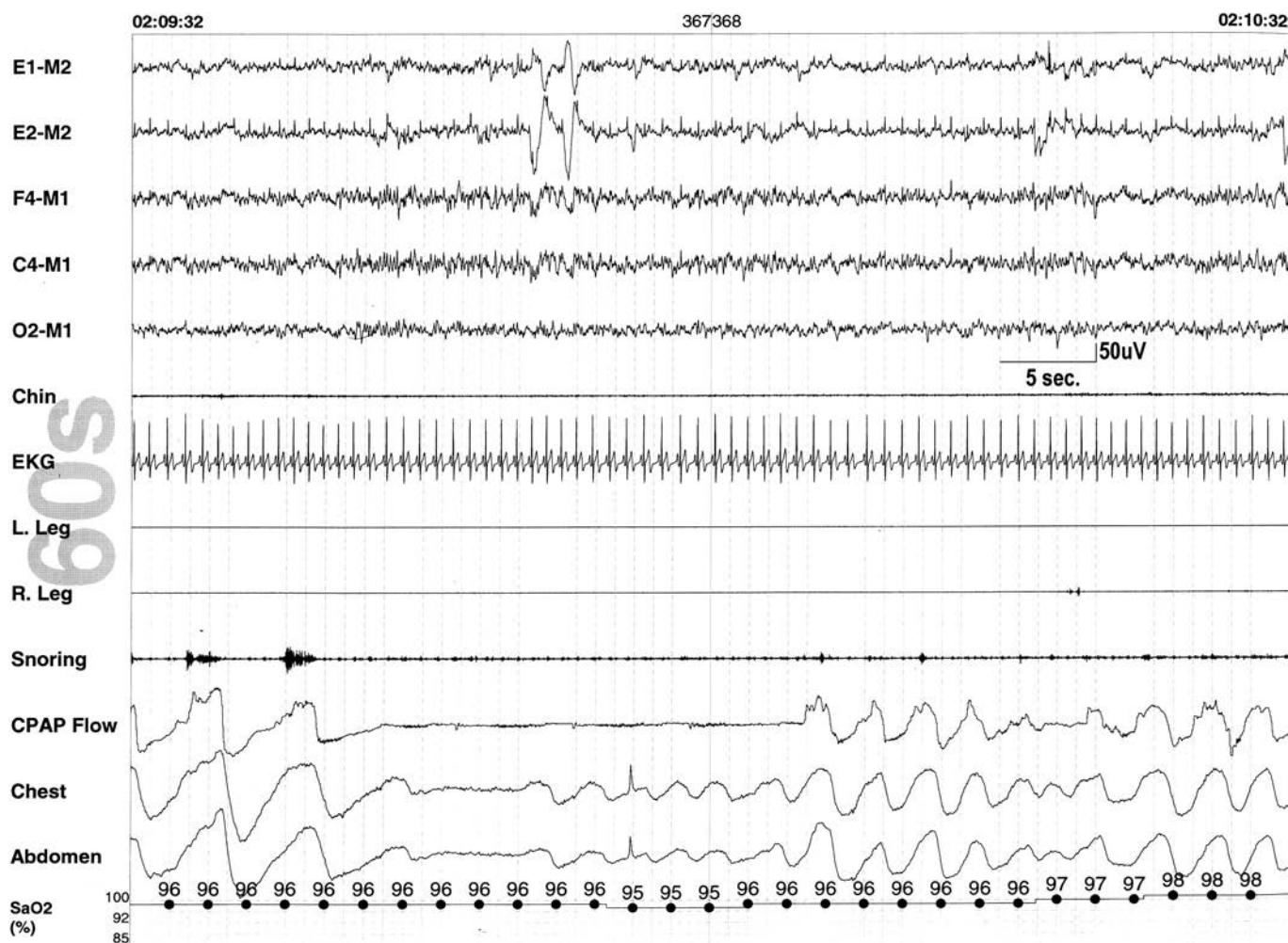
## MANAGEMENT AND TREATMENTS

Upon establishing a diagnosis of sleep apnea, the next step in the optimization of patient care is to determine the most appropriate and effective treatment available. A proper diagnosis includes determining the severity of the apnea (based on the AHI), which is also important in tailoring management to the individual patient. First, the patient is counseled on the preventative measures that should be implemented to assure their safety (i.e., avoiding tasks that necessitate attentiveness or operating a vehicle when tired) and are also given more information to help them better understand OSA.

### BEHAVIOR MODIFICATION

#### *Weight Loss*

As mentioned previously, almost all patients will have to change their lifestyle and be more cognizant of how OSA affects them. However, overweight or obese patients can see marked



**Figure 13-5.** An example of a mixed apnea showing central apnea with absence of chest and abdominal movements during first 50 seconds of apnea followed by 10 seconds of obstructive apnea. The resumption of respiration was associated with increased muscle artifacts and wake EEG pattern.

improvement in their symptoms with weight control.<sup>8</sup> Weight loss has been shown to decrease the apnea/hypopnea index, decrease daytime sleepiness, and improve overall sleep architecture.<sup>9</sup> A study comparing brief nutrition and exercise counseling (one session) and a more comprehensive weight loss plan including a low-calorie diet and a full year of exercise counseling demonstrated that the individuals who completed the more rigorous weight loss plan had a better quality of life

and ultimately a greater reduction in AHI and more significant weight loss.<sup>10</sup> The effects of weight loss on OSA obtained through bariatric surgery are still being evaluated, although various studies do support an improvement in AHI and overall BMI. However, the effects on quality of life, daytime sleepiness, and other associated factors have yet to be determined.

#### Body Position

In addition to evaluating for abnormal respiratory patterns and breathing pathology, polysomnography allows the clinician to observe a patient's position during sleep. There are a number of patients with OSA who have an exacerbation of their symptoms while lying supine. These patients are reportedly less likely to be overly obese and tend to be younger as well.<sup>11</sup> Changing to an alternative position (lateral recumbent) may improve symptoms of OSA and should be confirmed by seeing a normalization of AHI during polysomnography. Once corroborated, the positional change can be utilized as a primary therapy for OSA in this particular patient population. It should be mentioned that only one half of patients who are encouraged to sleep in the lateral recumbent position actually remain there. There are formal devices such as posture alarms, special

**TABLE 13.3**

**Associated Symptoms Found in Patients with OSA**

- Impotence and lowered libido
- Morning headaches
- Restless sleep
- Intermittent cessation of breathing during sleep
- Dry mouth
- Sore throat
- Elevation in daytime blood pressure
- Impaired concentration
- Nocturia
- Mood disorders
- Pulmonary hypertension

nightshirts, and specifically designed pillows that can be used to facilitate the transition to a new sleeping position. There are also makeshift devices such as placing tennis balls in a sock or altered t-shirts, or placing baseballs on the bed that can help to prevent the patient from moving back into the supine position. Efficacy is strongly correlated with compliance and tolerance of any of the aforementioned devices.

## MEDICATION AND ALCOHOL

Certain medications such as benzodiazepines, barbiturates, opiates, and other sedative drugs should be prescribed with caution as these can exacerbate symptoms of OSA. Patients who have been diagnosed with OSA should be alerted to the effects of significant alcohol consumption. Alcohol can promote weight gain, worsen sleepiness, depress the CNS, and ultimately exacerbate symptoms of OSA. Newer hypnotic drugs such as zolpidem, zaleplon, or eszopiclone are acceptable and may be better alternatives for patients with insomnia who suffer from OSA.

## POSITIVE AIRWAY PRESSURE

PAP is delivered through a nasal pillow, nose mask, or full face mask and improves OSA by maintaining patency of the airway via a compressed stream of air. The frequency, timing, and level of air pressure are calibrated to reduce respiratory events and at times associated snoring. There are three ways by which PAP therapy is administered:

1. Continuous positive airway pressure (CPAP) delivers air at a constant pressure that can be titrated to a certain level based on the needs of the patient. This pressure is determined during the sleep study, usually in the confines of a sleep center. The pressure can vary between 4 to 20 cm of water (cwp). Some patients require pressure as high as 30 cm of water. This is the first-line therapy for patients with OSA.
2. Bilevel positive airway pressure (BPAP) works by delivering both a set inspiratory PAP (IPAP) and an expiratory PAP (EPAP). While the former helps to facilitate inspiration by keeping the airway open, the latter pressure keeps the airway patent during exhalation. The EPAP pressure is set at least 4 cwp lower than the IPAP, making it a viable option for patients who have difficulty exhaling against CPAP. BPAP is often used when the patient cannot tolerate the CPAP pressure. BPAP may also be used for patients with central apnea when CPAP treatment is not successful.
3. Automatic positive airway pressure (Auto PAP) automatically determines the appropriate amount of pressure necessary to maintain an unobstructed airway. The PAP pressure requirement can vary throughout the night based on sleep stages, body position, medication or alcohol use, etc. The auto PAP delivers the minimum amount of pressure required for successful therapy, improving PAP use compliance in some patients.

## ORAL APPLIANCES

These include mandibular advancement splints and tongue-retaining devices that are ultimately designed to maintain a patent airway by holding the soft tissue of the oropharynx away

from the posterior pharyngeal wall. They have been shown to reduce the frequency of respiratory events and arousal in some patients with OSA; however, careful patient selection, severity of OSA, and compliance need to be taken into account prior to implementing this therapy.<sup>13</sup>

## SURGERY

As the most invasive option for the management of OSA, surgical intervention is practical for patients who have an identifiable obstructive pathology that is surgically correctable. Common procedures include uvulopalatopharyngoplasty, laser-assisted and radiofrequency ablation, rhinoplasty, septoplasty, tonsillectomy, adenoidectomy, tongue reduction procedures, and maxillomandibular advancement just to name a few. Nevertheless, surgery has not been proven as a primary treatment for those without a clear anatomic cause.

The management of OSA begins with a thorough history and then pertinent diagnostic evaluation through polysomnography. Treatment is a multidisciplinary approach that allows the clinician to tailor the patient's care based on their specific needs. Behavioral modification may be indicated for most, if not all patients with OSA, as lifestyle changes are crucial in assuring compliance and increasing the chance of treatment success. With regard to PAP, recent guidelines set by the American Academy of Sleep Medicine recommend starting PAP for individuals who have a RDI greater than 15 events per hour, or obstructive RDI between 5 and 14 events per hour with associated symptoms of OSA (snoring, daytime sleepiness, night-time awakenings, and breathing interruptions).<sup>14</sup> Generally, patients with moderate-to-severe OSA are started on PAP as first-line therapy. Patients who fall between mild and moderate can be tried on the various other therapies listed above; however, PAP still seems to be the most efficacious for those who can tolerate it.

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# Evaluating Narcolepsy and Related Conditions

## INTRODUCTION

Evaluating the cause of excessive daytime sleepiness (EDS) is the most common reason for patients to be referred for a laboratory-based sleep study. The vast majority of these patients will have or be suspected of having sleep-disordered breathing, most often obstructive sleep apnea (OSA). However, some patients may be sent for evaluation of other potential causes for EDS, such as narcolepsy, in which case the clinician may request a multiple sleep latency test (MSLT) to confirm the clinical diagnosis. Although not routinely indicated for the evaluation of other conditions associated with EDS, the MSLT may occasionally be used to differentiate idiopathic hypersomnia from narcolepsy, or in any condition in which it is necessary to document the degree of sleepiness. In the latter situation, a related technique, the maintenance of wakefulness test (MWT), may also be used. Whereas the MSLT measures one's tendency to fall asleep in a dark, quiet environment, the MWT is intended to objectively assess one's ability to maintain wakefulness in a nonstimulating environment for a given period of time. The tendency to fall asleep and the inability to stay awake are not the same thing; there is only a weak correlation between the MSLT and MWT in a population of sleepy subjects.<sup>1</sup> Hence, results from these studies may provide complementary information about patients with EDS.

It cannot be stressed strongly enough that both the MSLT and MWT must be performed and interpreted correctly if they are to be effective assessment tools. To quote the American Academy of Sleep Medicine (AASM) practice parameters,<sup>2</sup> these studies "...must be performed under appropriate conditions, using proper recording techniques and accepted protocols, with interpretation by a qualified and experienced clinician." Findings are useful only when considered within the entire clinical context, and in the case of the MSLT, are of diagnostic utility only when integrated with polysomnography (PSG) and other diagnostic information. They should be performed by experienced technologists and interpreted by sleep medicine specialists who have knowledge about both technical and patient-related issues that can affect the findings and interpretation.

## MULTIPLE SLEEP LATENCY TEST

### PRETEST PREPARATION

Mean sleep latency (MSL) is influenced by a number of factors, including prior sleep, medications, and patient activities. Sleep deprivation may affect MSL for several days after recovery sleep,<sup>3</sup> so it is recommended that patients keep a sleep log for at least 1 week prior to the study. Also, an overnight PSG must be performed the night before to exclude OSA or other causes of sleep fragmentation. A total sleep time (TST) of less than 6 hours on the preceding PSG may invalidate the results on MSLT for the diagnosis of narcolepsy, or at least would indicate that the study should be interpreted very cautiously. Many labs will not perform an MSLT ordered to diagnose narcolepsy if the TST falls below that level, or if the patient has an elevated arousal index or poor sleep efficiency, especially if they state that their sleep in the laboratory was more disturbed than at home. Ideally, stimulants, sedatives, and rapid eye movement (REM)-suppressing medications should be stopped at least 2 weeks before the MSLT. Regular medications may be continued, but their use must be carefully considered in advance by the sleep medicine clinician and clearly documented by the technologist, especially those medications that may have either alerting or sedating side effects. This is of particular importance for those taken on the day that the MSLT is performed. Drug screening is often done on the morning of the MSLT if there is suspicion that sleepiness may be pharmacologically induced or stimulants are being used (note, however, that modafinil is usually not detected in conventional drug screens). Caffeinated beverages should be avoided throughout the day of the test, and the patient should not smoke for at least 30 minutes before each nap. Other factors to avoid are vigorous physical activity and unusual exposure to bright light. A light breakfast is recommended before the first nap (at least an hour before), and a light lunch should be consumed immediately after the second midday nap.

### PERFORMING THE MSLT

The MSLT typically consists of 5 nap opportunities performed at 2-hour intervals during the patient's normal waking hours

(an important issue to bear in mind for shift workers). The first nap opportunity should begin 1.5 to 3 hours after the patient spontaneously awakens from the PSG. Note that it is recommended that an MSLT is not performed after a “split night” sleep study [combined diagnostic PSG and positive airway pressure (PAP) titration], as a change in the usual pattern of sleep (for either better or worse) that may accompany the introduction of PAP would invalidate the study. A shorter 4-nap version of the MSLT is sometimes performed, but the results may not be reliable for diagnosing narcolepsy (see “Scoring and Interpreting the MSLT”). Patient rooms should be dark and quiet, and the room temperature set for patient comfort.

The montage typically used for the MSLT consists of a minimum of 2 EEG channels (C3/4-A2/1 and O1/2-A2/1). We have been including F3/4-A2/1, as in the montage recommended for recording PSGs in the recent AASM scoring manual.<sup>4</sup> In addition, left and right electrooculogram (EOG), submental/mental EMG, and EKG are recorded. Prior to each nap opportunity, the patient’s comfort should be assessed (including allowing him or her to use the toilet as needed). Once this is done, the following instructions are given to the patient for biocalibrations:

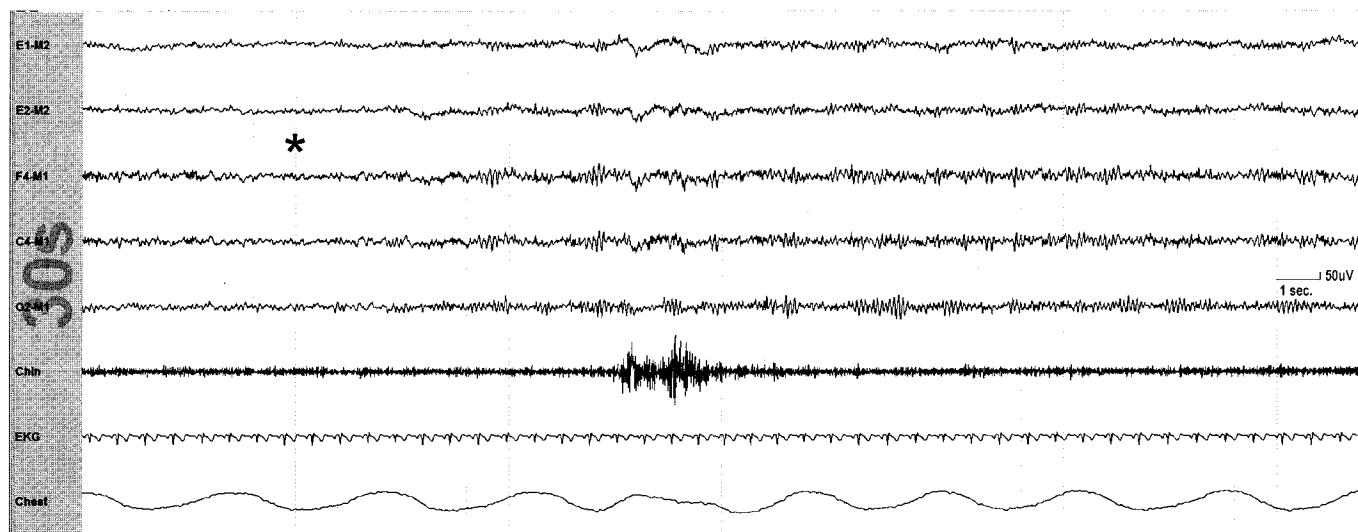
- “Lie quietly with your eyes open for 30 seconds.”
- “Close both eyes for 30 seconds.”
- “Without moving your head, look to the right, then left, then right, then left, then right, then left.”

- “Blink eyes slowly five times.”
- “Clench or grit your teeth tightly together.”
- “Please lie quietly, assume a comfortable position, keep your eyes closed, and try to fall asleep.”

The lights are then turned off, indicating that the test has begun. Between naps, the patient should be instructed to get out of bed and perform nonstimulating activities until the next nap opportunity begins.

## CONCLUDING THE TEST

“Clinical” and “research” MSLT protocols have been developed that specify criteria for nap termination and determination of sleep onset, but only the former will be discussed here. Individual naps are concluded after 15 minutes of any sleep. Note that this is the total elapsed time from the onset of sleep and not TST; it is unnecessary for the technologist to keep track of the cumulative duration of sleep during naps. Also, naps are concluded if there has been no sleep for 20 minutes. After the final nap, any patient with a low MSL (see below) should be instructed either not to drive at all or to drive only with extreme caution and only when not feeling sleepy. However, it should be borne in mind that there are conflicting data on the relationship between MSLT results and motor vehicle crashes.<sup>5–7</sup> It is our practice to routinely warn ANY PATIENT who reports EDS to exercise caution regarding driving (or other potentially



**Figure 14-1.** This 30-second epoch is scored as stage W (wake), as less than 15 seconds is composed of features characteristic of N1. A “microsleep” with decreased alpha is indicated by the asterisk.

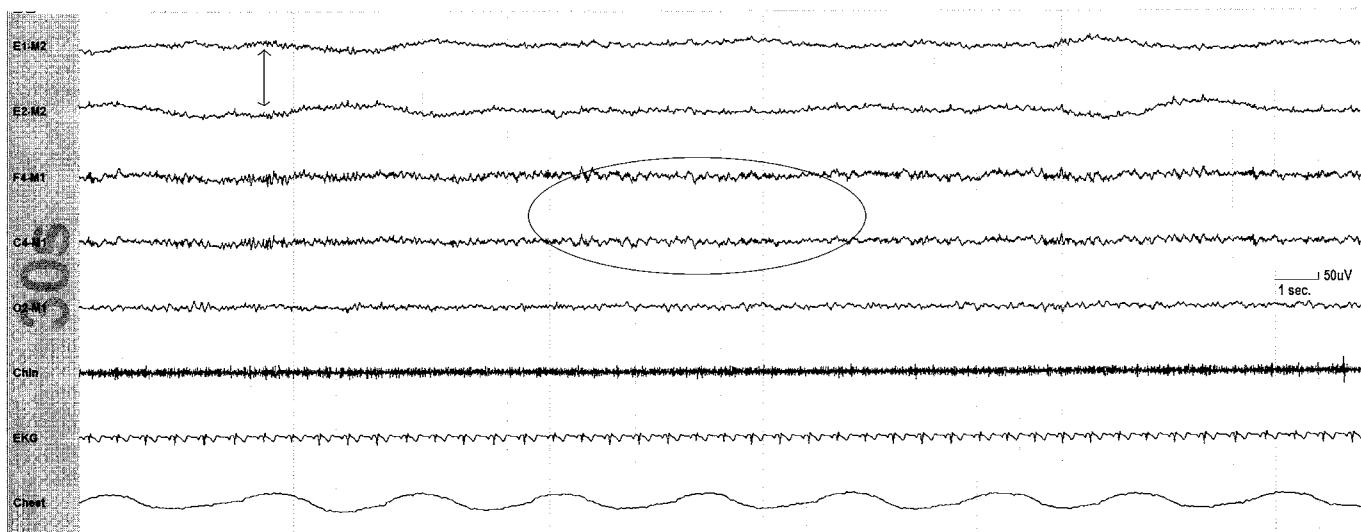
dangerous activities) regardless of his or her MSL. Those patients who report a history of sleepiness-related crashes (or near misses) or have MSL less than 5 minutes should be told that they must not drive unless authorized by their physician.

### SCORING AND INTERPRETING THE MSLT

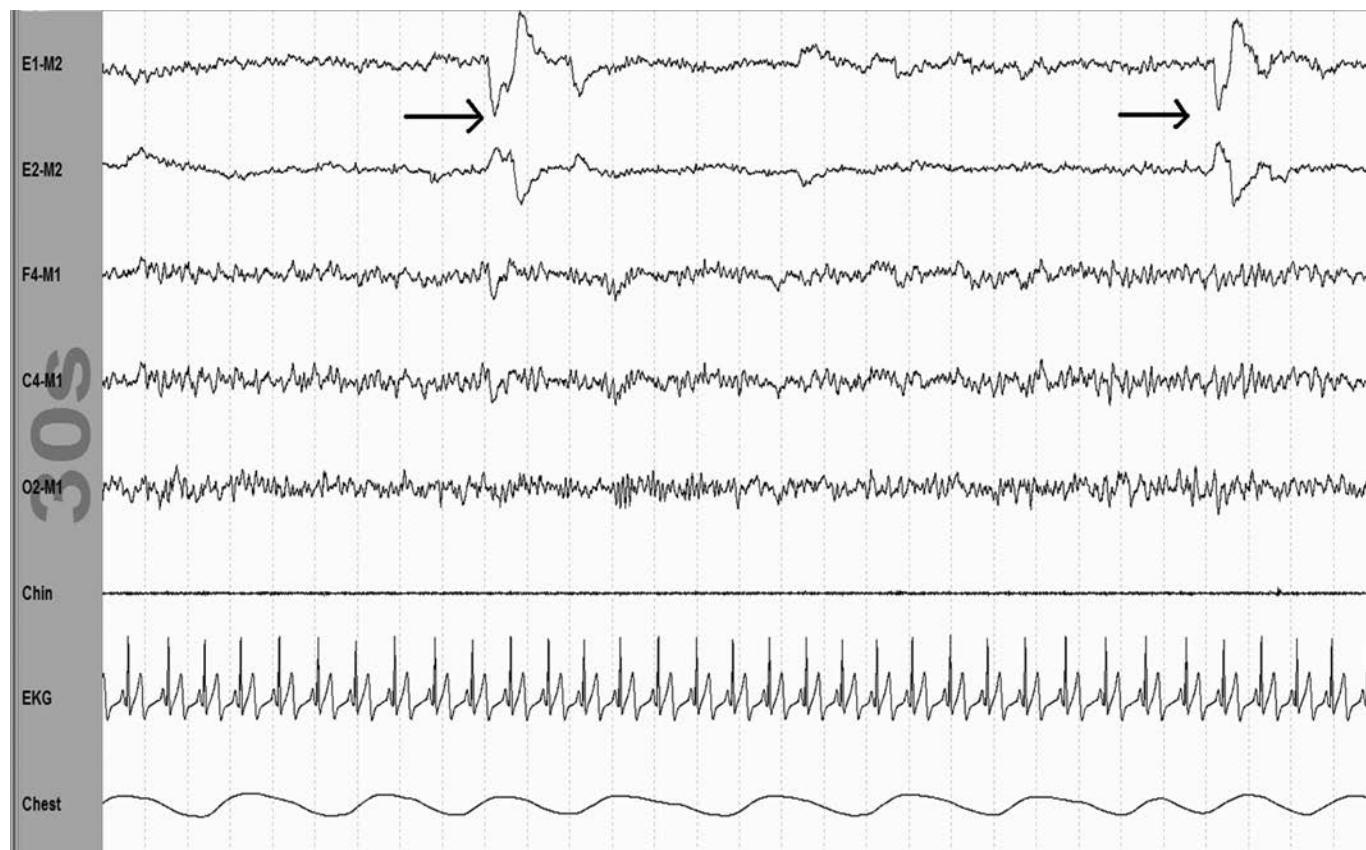
Sleep onset is determined from “lights out” to the first epoch of any stage of sleep. Remember that at sleep onset, patients typically have “microsleeps” characterized by brief intrusions of “N1” EEG patterns (absence of alpha and increased theta) and occasional slow-rolling eye movements (SEMs) (Fig. 14-1). During the sleep onset period, there may be several epochs containing microsleeps before an epoch of scorable N1 occurs (Fig. 14-2). However, unless 15 or more seconds of a typical 30-second epoch have these features, it cannot be scored as N1. The 15 seconds do not have to be contiguous; so, as long as a total of 15 seconds with typical features of N1 is recorded, the epoch may be scored as such. The sleep onset latency (SL) in minutes for each nap is determined by counting the number of epochs of wakefulness (starting with the epoch after the one in which “lights out” occurred) before the first epoch of sleep and dividing the result by 2. For example, if “lights out” occurred in epoch 55, epochs 56 to 61 were those of wakefulness (stage “W”), and the first epoch of N1 was in epoch 62, the SL is 3 minutes (6 epochs/2 = 3). The MSL is calculated by taking the arithmetic mean of the latencies for the 5 naps (20 minutes is used for a nap opportunity in which the patient did not sleep).

REM (stage R) latency is determined by counting all epochs of non-REM sleep (and wakefulness) from the first epoch of sleep to the last one before the first epoch of stage R. An example of an epoch of stage R, as it appears on an MSLT, is shown in Figure 14-3. If the first epoch of sleep occurred in epoch number 62 and stage R appears for the first time in epoch 76, the stage R latency would be 7 minutes (14 epochs/2 = 7). Remember that all epochs that occur after sleep onset, including those with any stage of sleep and stage W, are counted when determining stage R latency. Any nap containing stage R is referred to as a “sleep-onset REM period” (or “SOREMP”). It is important that epochs of N1 with SEMs are not confused for stage R, although this differentiation can sometimes be a bit challenging (Fig. 14-4). As a rule, the duration of the initial deflection of an SEM should be greater than 500 milliseconds, while it is typically less than that for an REM. MSLT reports should include start and end times of each nap opportunity, latency for each nap, the MSL, and the number of SOREMPs. Any deviations from the standard protocol should also be recorded. A sample work sheet that we use in our laboratory is shown in Figure 14-5 (note that the example given above is taken from nap No. 2).

Unfortunately, there is no large systematically collected body of normative data for MSLs. There is a wide range in MSLs for both normal control subjects as well as patients with narcolepsy and OSA, making it difficult to establish a normal cut-off value. Most centers agree that MSLs less than 5 should be considered abnormal and greater than 10 normal. Many regard 5 to 10 as



**Figure 14-2.** This epoch is scored as unequivocal N1 with increased theta (*indicated by an oval circle*) and slow eye movement (*an example is indicated by the arrow*).



**Figure 14-3.** This epoch is scored as stage R with REM (an example is indicated by the arrow) and absence of muscle tone at chin EMG channel.

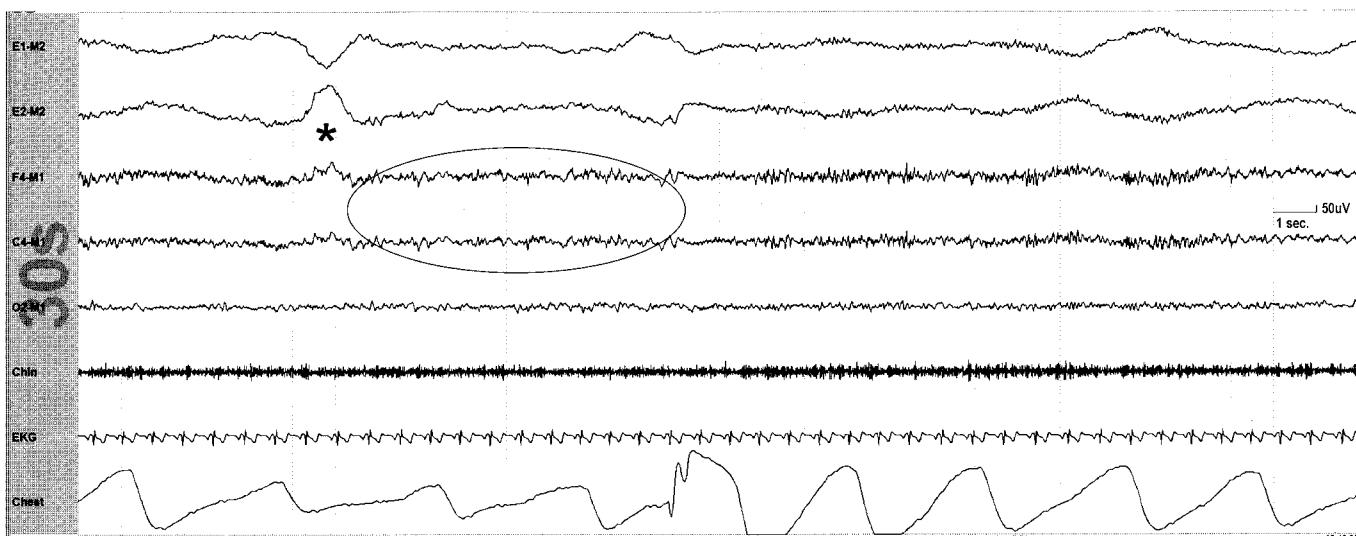
"indeterminate," while others consider values less than 8 as abnormal, the latter being the value used in the latest edition of the International Classification of Sleep Disorders, the ICSD-2.<sup>2</sup> Using a cut-off of 8 minutes provides high sensitivity for picking up excessively sleepy patients (~95%), but the specificity drops from 90% to 73% (compared to a 5-minute cut-off). This means that when values less than 8 minutes are considered abnormal, nearly all patients who are pathologically sleepy will be detected, but about one out of four of those who are not excessively sleepy will be incorrectly identified as being abnormal. Even with a 5-minute cut-off, about 16% of normal subjects will fall into the "abnormal" range.<sup>8</sup> MSLs are normally distributed, but the standard deviations (SDs) are relatively large; using 2 SDs as the cut-off, a "normal" MSL would be as low as 2 minutes! This is why the results of the MSLT have to be interpreted cautiously within the context of the patient's clinical history, ensuring that potentially confounding factors are rigorously eliminated or at least identified. Patients with "abnormal" MSLs should be labeled as having objective evidence of hypersomnolence or EDS only when the study is meticulously performed according to protocol and after careful attention has been paid to all key clinical features. Contrariwise, those with "normal" results may still be excessively sleepy and could be at risk for motor vehicle crashes and other injuries. It should be recalled that a normal MSLT

does not rule out narcolepsy; it is not uncommon for narcoleptics with normal results to be abnormal on a second study.

SOREMPs are common in patients with narcolepsy; but almost one out of four will not have the two or more typically used to support the diagnosis on a single MSLT.<sup>9</sup> Regardless of the cause of a patient's EDS, the number of SOREMPs tends to increase with shortening of the MSL, and it is important to recall that as many as 7% of patients with OSA will have two or more SOREMPs. If a 4-nap MSLT is done, a minimum of two SOREMPs should always be used as a standard for confirming the diagnosis of narcolepsy (the ICSD-2 requires two SOREMPs in all cases).

#### INTERPRETATION PITFALLS

The interpreting clinician must be ever mindful of the factors that can spuriously affect MSLs. For example, chronically sleep-deprived individuals or those who are by nature long sleepers may meet criteria for narcolepsy if awakened early from the preceding night's PSG by lab personnel (usually for convenience). Even a single "ad lib" night of "normal" sleep may not be enough to reverse the effects of chronic sleep deprivation in some patients (which may actually take several nights). On the other hand, MSLs are prolonged if patients are allowed to do physical activity before naps; even just a 5-minute walk can have a



**Figure 14-4.** This is an epoch of N1 with predominant theta activity indicated by the *oval circle*, but the eye movements might confuse a less experienced scorer. Although the eye movement indicated by the *asterisk* is rather sharply contoured, REMs should have an initial deflection of less than 500 milliseconds (see Fig. 14-3). The initial deflection of this eye movement is just over 1 second, making it an SEM. The high chin EMG level is also a clue that this is an epoch of N1 and not stage R. There is intermittent theta background activity shown by *oval circle*.

meaningful effect.<sup>10</sup> MSLs are also prolonged by anxiety (including the “I’m outta here” phenomenon that occurs with some patients in anticipation of going home later in the afternoon). As discussed earlier, there is a difference between being excessively sleepy and having “high sleepability.” That is, there are some individuals with MSLs below 8 minutes who are perfectly able to maintain wakefulness when necessary and are not pathologically sleepy. There are limited normative data for different age groups (most studies have been done in healthy young adults); so, when studying children or the elderly, who tend to have longer MSLs, one has to interpret results more cautiously.<sup>11</sup> Finally, several studies have shown a difference in MSLs between the 4- and 5-nap protocols (MSLs are typically longer for the 5-nap version). Hence, one should be especially careful not to overinterpret a borderline abnormal 4-nap study.

## MAINTENANCE OF WAKEFULNESS TEST

In contrast to the MSLT, which attempts to measure one’s tendency to fall asleep, the MWT is intended to test one’s ability to stay awake. These are quite distinctly different functions. The MWT is most often done to assess fitness for duty in persons whose occupation requires a high degree of certainty that they can stay awake (e.g., truck drivers and pilots). It is also sometimes used to assess response to treatment in complicated cases, such as those with both narcolepsy and OSA. In addition, the MWT is widely used as a measure of response to treatment in research studies.

### PROCEDURE

In many ways, the MWT procedure is similar to that of the MSLT, except that a preceding PSG is usually not performed.

Also, unlike the MSLT, four rather than five trials are performed (note that the word “trial” is used instead of “nap” as the goal of the MWT is to see if the patient is able to stay awake rather than fall asleep!). The first trial should begin 1.5 to 3 hours after the patient’s habitual wake-up time (for most people, this will be about 9 to 10 AM). Although a 20-minute trial length has been used by some centers in the past, the 40-minute protocol is preferred as results are more normally distributed due to less of a “ceiling effect” that tends to be seen when the shorter trial duration is used.<sup>8</sup> As with the MSLT, the patient room should be quiet and shielded from external light, and the room temperature adjusted for patient comfort. A light source in the room should be placed just behind the patient’s head so as to be just out of the patient’s field of vision. A recommended arrangement is to place a 7.5 W night-light 1 foot off the floor and 3 feet lateral to the patient’s head. The patient is then allowed to sit up in bed with head and back supported by pillows, and the neck should be adequately supported in a comfortable, neutral position. Attention to meals, use of the toilet and other issues of patient comfort, as well as biocalibrations are the same as with the MSLT. Prior to turning out the overhead light, the patient is given this instruction: “Please sit still and remain awake for as long as possible. Look directly ahead of you, and do not look directly at the light.” Patients are admonished to refrain from using extraordinary measures to stay awake (e.g., slapping their faces!).

Pretest preparation is different in some ways from the MSLT; there is no consensus as to whether it is necessary to use sleep logs before an MWT or whether patients should be instructed to abstain from smoking, using caffeine, and taking medications before and during the MWT. As the MWT is intended to show one’s ability to remain awake in a “normal” daily pattern,

### Multiple Sleep Latency Test: Data Collection and Report Form

Name PATIENT, TEST Hosp# 99-9999-9 Date 6/10/09 DOB 1/15/81

MSLT# 222 Room# 13 Computer Drive E

	Nap #1	Nap #2	Nap #3	Nap #4	Nap #5
Scheduled Time	0730	0930	1130	1330	1530
Start Time	0727	0926	1121	1321	1514
Start Epoch	5	55	97	138	189
Sleep Onset Epoch	17	62	103	155	214
Sleep Latency (mins.)	5.5	3	2.5	8	12
REM Onset Epoch	—	76	111	—	—
REM Latency (mins.)	—	7	4	—	—
Sleep Stages	1, 2	1, 2, R	1, 2, R	1, 2	1
Comments					

Mean Sleep Latency =  $31/5 = 6.2$  Mean REM Latency =  $11/2 = 5.5$  Scoring Tech JW

**Figure 14-5.** Sample of the technologist worksheet used for MSLTs at the University of Iowa. Note that the example for determining sleep-onset and REM latencies described in the text is taken from nap No. 2.

some clinicians prefer having patients behave in a manner that is similar to the way they would in a regular day. As with the MSLT, a drug screen (including serum caffeine level) may be necessary on the morning of the MWT to confirm that stimulants are not being used to promote wakefulness.

Sleep onset is determined as with the MSLT. Some laboratories have used “unequivocal sleep” (i.e., three consecutive epochs of N1 or deeper sleep) for determining sleep onset, although the current recommendations are to use the first epoch that has been scored as any sleep. Trials are ended after 40 minutes if no sleep is recorded, or after “unequivocal sleep.” MSL is calculated as in the MSLT. As with the MSLT, technologists should record start and stop times for each trial, individual sleep latencies, stages of sleep attained during each trial, and any deviations from the standard protocol.

#### INTERPRETATION

Due to the fact that MSLs on the MWT are not “normally distributed,” the value used to determine abnormality is rather arbitrary. Most centers consider MSLs less than 8 as abnormal. However, according to the AASM practice parameters,<sup>12</sup> “Stay-ing awake on all trials of a 40 minute MWT provides the stron-

gest objective data available supporting an individual’s ability to stay awake and may provide an appropriate expectation for individuals requiring the highest level of safety.” Although an MSL of less than 8 minutes may be “abnormal” and 40 minutes “the strongest objective data” supporting one’s ability to stay awake, observed values often fall between 8 and 40 minutes and, hence, are relegated to being labeled “of uncertain significance.” Note that only 59% of normal subjects are able to remain awake in all four trials using the protocol described above.<sup>13</sup> Although the MWT may be useful for determining one’s ability to stay awake in certain circumstances, there is a considerable amount of imprecision in that determination, and the interpreting physician should remain circumspect about declaring a particular patient either “fit” or “unfit” based on the MWT alone.

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# Parasomnias

## INTRODUCTION

The International Classification of Sleep Disorders, second edition, *Diagnostic and Coding Manual* (ICSD) published in 2005, describes parasomnias as undesired physical phenomena that occur during entry, within, or upon arousal from sleep.<sup>1</sup> They are usually associated with a state of central nervous system (CNS) activation, evidenced as an elevation of autonomic and skeletal muscle activity, often with an experiential element.

Four “basic drive” states can emerge in pathological forms as discrete parasomnia events. Three of these states are referred to as “appetitive behaviors” (sleep, feeding, and sex), while the fourth is aggression. In the ICSD, there are 15 core parasomnias that have been divided into three major categories: the Disorders of Arousal (From NREM Sleep), the Parasomnias Usually Associated with REM Sleep, and a final category, the Other Parasomnias (Table 15.1).

## POLYSOMNOGRAPHY

The Dement and Kleitman original description in 1957 of the major electrophysiological concomitants of sleep [a combination of electroencephalogram (EEG), electro-oculogram (EOG), and electromyogram (EMG)] allowed for the present-day polysomnogram (PSG) description of three specific sleep stages from non-rapid eye movement (NREM) and rapid eye movement (REM) sleep; stage N1 (NREM 1), stage N2 (NREM 2), stage N3 (NREM 3), and stage R (REM) sleep.<sup>2,3</sup> As evidenced by the ICSD designations “Disorders of Arousal (From NREM Sleep)” and “Parasomnias Usually Associated with REM Sleep,” a large number of parasomnias are associated with specific sleep stages, especially stages N3 and R sleep (Figs. 15-1 and 15-2).<sup>4</sup>

This can prove useful when taking the sleep history. Normally, much of the first third of a normal night’s sleep is spent in stage N3 sleep, whereas the last third of the night is largely spent in stage R sleep (Fig. 15-3). Documenting consistent behaviors soon after sleep onset or just before waking in the morning can help narrow the differential diagnosis.

Although a single night PSG may not capture the parasomnia under investigation, there are frequent PSG correlates that can often suggest the diagnosis. When a parasomnia is captured during a sleep study, close attention by the technologist should be focused on the concomitant PSG data and clinical presentation immediately prior to, during, and following the event. As parasomnias are undesirable physical phenomena often associated with CNS activation (evidenced as elevated autonomic and skeletal muscle activity), the differential diagnosis frequently includes seizures and a variety of sleep-related movement disorders not otherwise classified as parasomnias. The documentation of a specific sleep stage, an ictal (seizure) EEG pattern, and behaviors characteristic of a parasomnia or seizure with split-screen, video-PSG is mandated for accurate diagnosis.

**TABLE 15.1** Parasomnias

### DISORDERS OF AROUSAL (FROM NREM SLEEP)

1. Confusional Arousals
2. Sleepwalking
3. Sleep Terrors

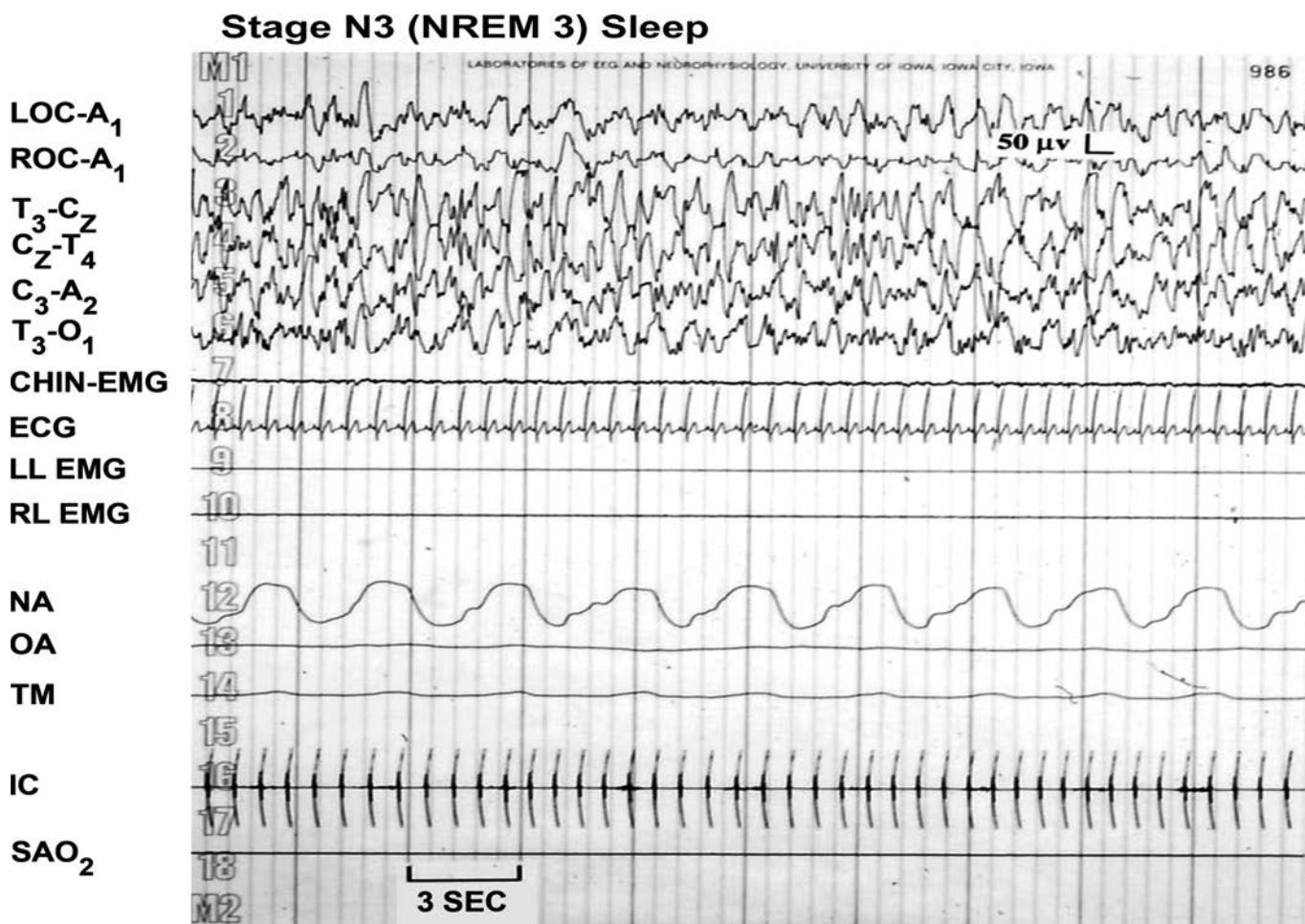
### PARASOMNIAS USUALLY ASSOCIATED WITH REM SLEEP

4. REM Sleep Behavior Disorder (*Including Parasomnia Overlap Disorder and Status Dissociatus*)
5. Recurrent Isolated Sleep Paralysis
6. Nightmare Disorder

### OTHER PARASOMNIAS

7. Sleep-Related Dissociative Disorders
8. Sleep Enuresis
9. Sleep-Related Groaning (*Catathrenia*)
10. Exploding Head Syndrome
11. Sleep-Related Hallucinations
12. Sleep-Related Eating Disorder
13. Parasomnia, Unspecified
14. Parasomnia Due to Drug or Substance
15. Parasomnia Due to Medical Condition

*Source:* Adapted from American Academy of Sleep Medicine. *International Classification of Sleep Disorders*, 2nd ed. Diagnostic and Coding Manual. Westchester, IL: American Academy of Sleep Medicine, 2005.



**Figure 15-1.** Stage N3 (NREM 3) sleep is scored on a PSG tracing when  $\geq 20\%$  of a 30-second epoch (at a sweep speed of 10 mm/s) comprises frontally dominant delta wave forms [high voltage ( $> 75 \mu\text{V}$ ), frequency = 0.5–2 Hz]. (A<sub>1</sub>, left ear; C, central; ECG, electrocardiogram; EMG, electromyogram; IC, intercostal EMG; LOC, left outer canthus; LL, left leg; NA, nasal airflow; O, occipital; OA, oral airflow; RL, right leg; ROC, right outer canthus; SAO<sub>2</sub>, oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neural* 2001;21:377–390; Fig. 4, with permission.)

## SPECIFIC PARASOMNIAS

### TYPES OF PARASOMNIAS

#### *Disorders of Arousal (From NREM Sleep)*

**CONFUSIONAL AROUSALS.** Confusional arousals are spells that last from minutes to hours and generally arise from stage N3 sleep. There are two types: one occurs relatively early after sleep onset and is seen more frequently in children, and the second occurs in the morning and is more common in adults.<sup>1</sup>

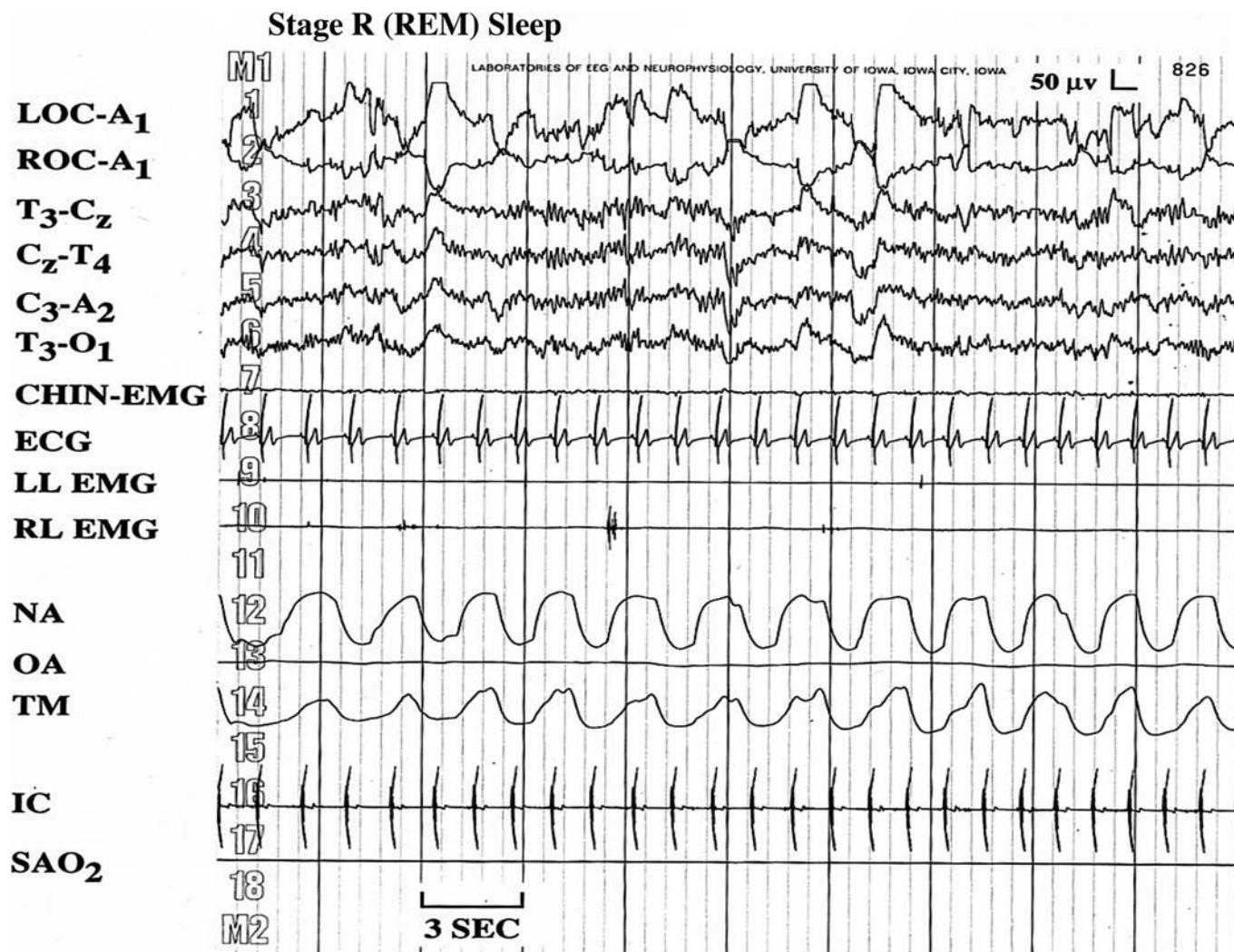
Although confusional arousals are relatively common and benign in children, they may predispose to adolescent sleep-walking.<sup>1</sup> In addition, especially in adults, violent behavior for which the patient is amnestic can occur if there is an external attempt to fully awaken them during an event. Two variants of the adolescent/adult type of confusional arousal are severe morning sleep inertia (sleep drunkenness) that mainly arises from light NREM sleep, and sleep-related abnormal sexual behaviors (sexsomnia) associated with abnormal sexual, at times assaultive behavior.<sup>1,5,6</sup>

The prevalence of confusional arousals in the age group three to 13 years has been reported to be 17.3%, whereas in adults it may reach 4.2%.<sup>1</sup> A genetic predisposition to confusional arousals can be amplified by a variety of stressors that include insufficient sleep and drug use.<sup>7</sup>

**Case No. 1:** A 45-year-old woman with significant psychosocial stresses presented with arousals from sleep associated with confusion and panic.<sup>4</sup> A PSG captured one of her typical spells. This event occurred suddenly as she sat up during stage N3 sleep (Fig. 15-4). The split-screen video analysis allowed the appreciation of her frightened and confused countenance.

**Case No. 2:** A 20-year-old male with severe intellectual disability (mental retardation) had a history of nocturnal self-injurious behavior.<sup>4</sup> In the laboratory, a confusional arousal from stage N3 sleep was captured, during which there was a persistent EEG pattern indicating sleep, despite an increase in muscle artifact and behavior that might otherwise have suggested wakefulness (Fig. 15-5).

**SLEEPWALKING.** Sleepwalking (somnambulism) frequently occurs in children previously diagnosed with confusional



**Figure 15-2.** Stage R (REM) sleep is scored on a PSG tracing when over 50% of a 30-second epoch (at a sweep speed of 10 mm/s) shows a relative marked reduction in EMG activity with occasional bursts of muscle activity and REMs, a background EEG activity of relatively low-voltage, mixed frequency activity with slow alpha/theta patterns, and intermittent saw-tooth waves (2–6 Hz, centrally prominent “sawtooth wave” discharges). (A<sub>1</sub>, left ear; C, central; ECG, electrocardiogram; EMG, electromyogram; IC, intercostal EMG; LOC, left outer canthus; LL, left leg; NA, nasal airflow; O, occipital; OA, oral airflow; RL, right leg; ROC, right outer canthus; SAO<sub>2</sub>, oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Fig. 5, with permission.)

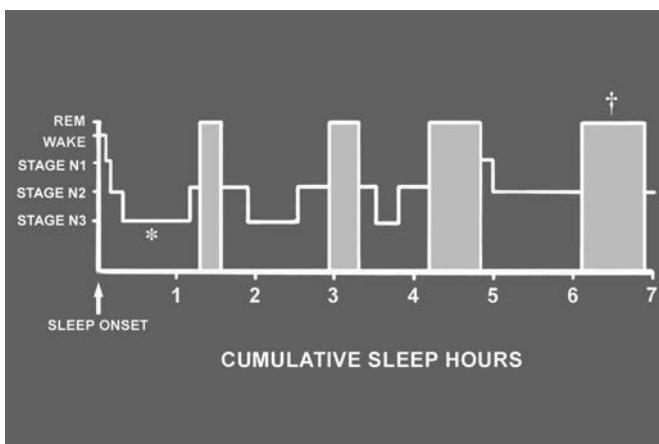
arousals.<sup>1</sup> In childhood, sleepwalking has a prevalence of up to 17%, peaking between eight to 12 years of age, with a strong genetic factor in 65%.<sup>1,8</sup> Although it usually resolves by puberty, sleepwalking affects an estimated 4% of the adult population where violent behavior and injuries occur more frequently in men.<sup>9</sup> Sleepwalking classically arises from stage N3 sleep, usually at the end of the first or the second period of slow wave sleep.

**Case No. 1:** A 22-year-old college student under significant stress was amnestic of the confusional arousals and nocturnal wanderings witnessed by her roommates.<sup>4</sup> Her PSG captured multiple confusional arousals from stage N3 sleep associated with standing and attempting to walk (Fig. 15-6). The technologist reported her as confused and requiring repeated gentle redirection back to bed, after which she quickly fell back into sustained clinical and electrographic sleep. Upon interview the morning following this study, the patient was amnestic of all observed events.

**SLEEP TERRORS.** Sleep terrors, sometimes referred to as *pavor nocturnus* in children and as *pavor incubus* in adults, are abrupt episodes that arise from sleep in association with marked autonomic hyperactivity, as evidenced by diaphoresis and tachycardia, and extreme fear, often with hysterical screaming and crying.<sup>1</sup> The onset is usually between 4 and 12 years of age, with a prevalence of up to 6.5% in children.<sup>10</sup> Although sleep terrors generally resolve in adolescence, the prevalence in adults up to 65 years may reach 2.6%.

Although not associated with psychopathology in children, sleep terrors in adults on occasion have been reported in patients with bipolar, depressive, and anxiety disorders.<sup>11</sup> On PSG, sleep terrors characteristically arise toward the end of the first or the second period of stage N3 sleep.<sup>1</sup>

**Case No. 1:** A 16-year-old girl presented with recurrent spells from sleep associated with combative behavior, with a concern for nocturnal seizures. During one event, she reportedly fell



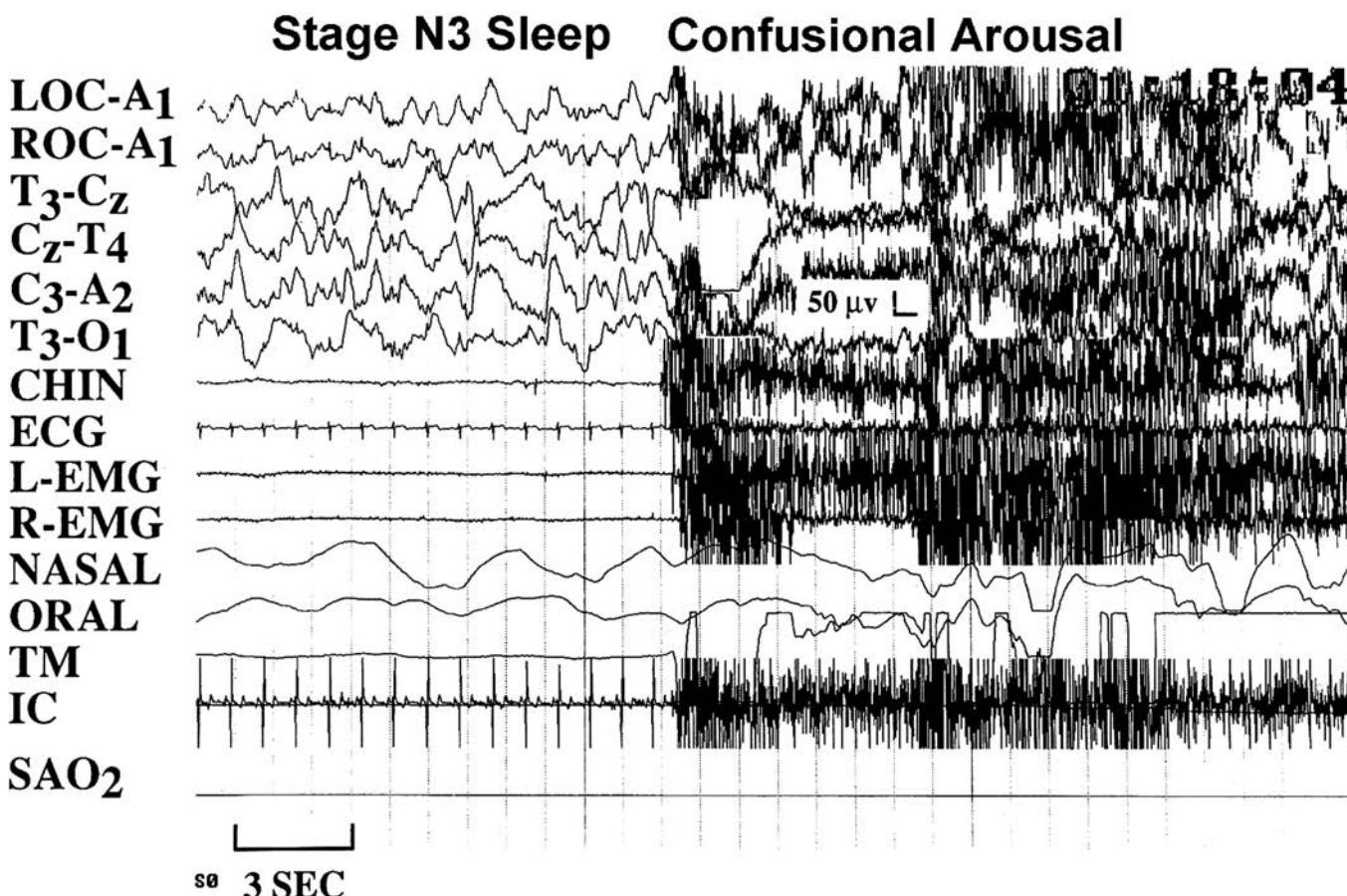
**Figure 15-3.** This histogram shows the general progression of sleep stages throughout a relatively normal night of sleep in a young adult, with the majority of consolidated stage N3 sleep occurring early in the night (as depicted by the asterisk) and the majority of consolidated/relatively prolonged stage R sleep occurring in the early morning hours (as depicted by the dagger) relatively close to the expected waking time. (\* = early evening stage N3 sleep; † represents late evening/early morning stage R sleep.) (Modified from the educational slide set “Sleep Disorders”; Scope Publications, The Upjohn Company, 1983.)

down the stairs and chipped some teeth. A PSG captured one of her classical events that arose from stage N3 sleep. She immediately began to tear off her electrodes and attempted restraint by the technologist exacerbated the relatively violent behavior; later the patient was completely amnestic of the event.

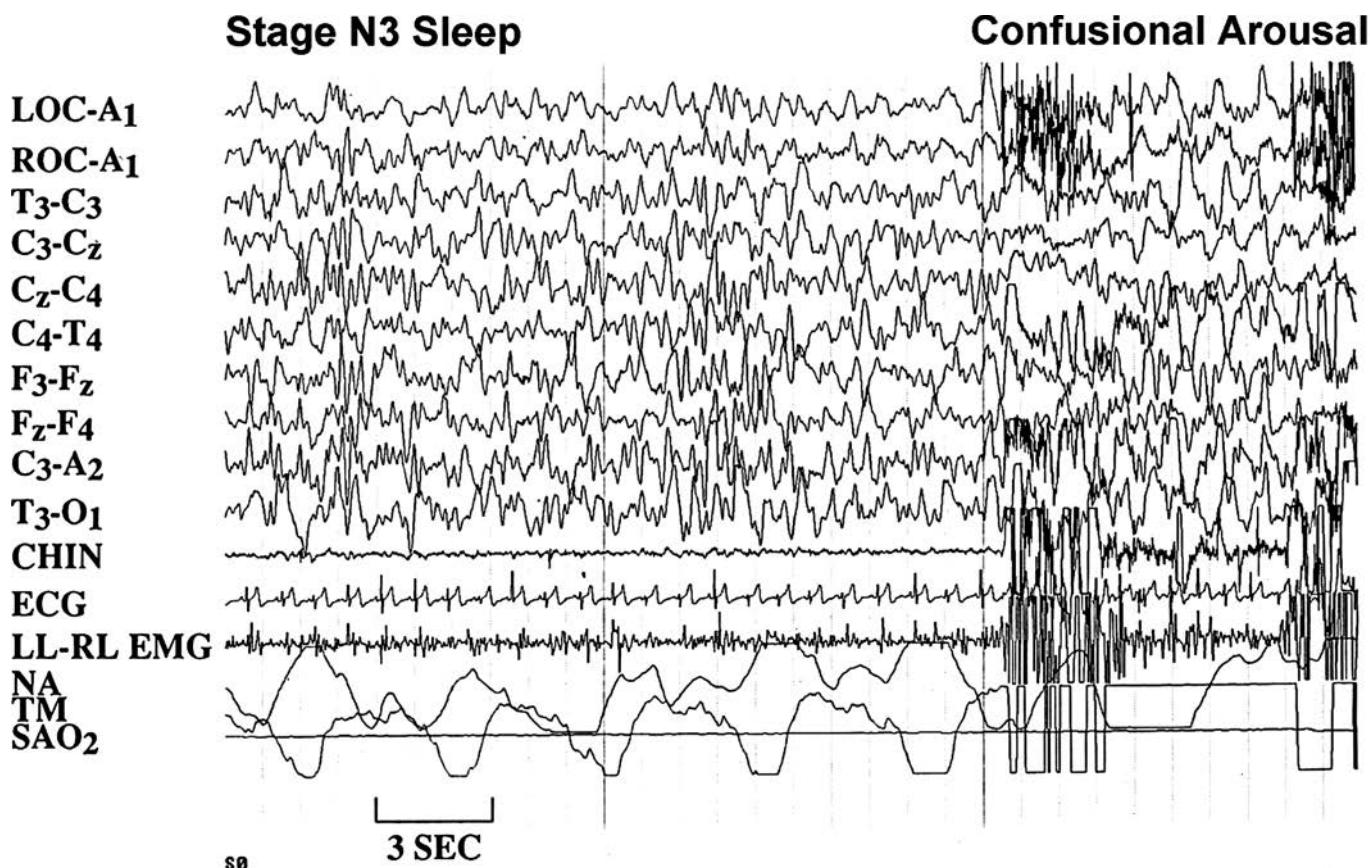
#### Parasomnias Usually Associated with REM Sleep

**REM SLEEP BEHAVIOR DISORDER.** The REM sleep behavior disorder (RBD) occurs most frequently in elderly males during stage R sleep.<sup>1,12</sup> It is associated with directed violent behaviors that are followed by an arousal in which the patient can describe a dream that corresponds with previously observed movements. This phenomenon is known as *isomorphism*.<sup>1</sup> Dream-related injuries are reported in up to 77.1% of individuals with RBD.<sup>1,13</sup>

The prevalence of RBD in the general population ranges from 0.38% to 0.8%.<sup>1</sup> Although the full parasomnia is only captured by PSG in 8%, the ICSD laboratory diagnostic criteria only demand an unusual elevation of EMG activity (muscle tone) during stage R sleep, a finding referred to as *REM without atonia* (Fig. 15-7).<sup>1,4,14</sup> Another frequently observed PSG finding is periodic limb movements in sleep (PLMS), in up to 75% of patients.<sup>1</sup>



**Figure 15-4.** The PSG of a 45-year-old woman with a history of confusional arousals associated with panic clearly showed the classic association with stage N3 sleep. (A<sub>1</sub>, left ear; C, central; ECG, electrocardiogram; EMG, electromyogram; IC, intercostal EMG; LOC, left outer canthus; L, left leg; O, occipital; R, right leg; ROC, right outer canthus; SAO<sub>2</sub>, oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Fig. 13, with permission.)



**Figure 15-5.** A young man with profound intellectual disability (mental retardation) and nocturnal self-injurious behavior demonstrated a brief confusional arousal from stage N3 sleep, during which he struck himself in the head. (A<sub>1</sub>, left ear; C, central; ECG, electrocardiogram; EMG, electromyogram; F, frontal; LOC, left outer canthus; LL, left leg; NA, nasal airflow; O, occipital; RL, right leg; ROC, right outer canthus; SAO<sub>2</sub>, oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Fig. 12, with permission.)

RBD can be the initial manifestation of a group of neurodegenerative disorders known as *synucleinopathies*, which are characterized by Parkinson's disease.<sup>2,4,15</sup> An estimated 33% of newly diagnosed patients with Parkinson's disease have RBD, and approximately 66% of men over 50 years of age with RBD will develop Parkinson's disease within 13 years of their RBD diagnosis.<sup>1</sup>

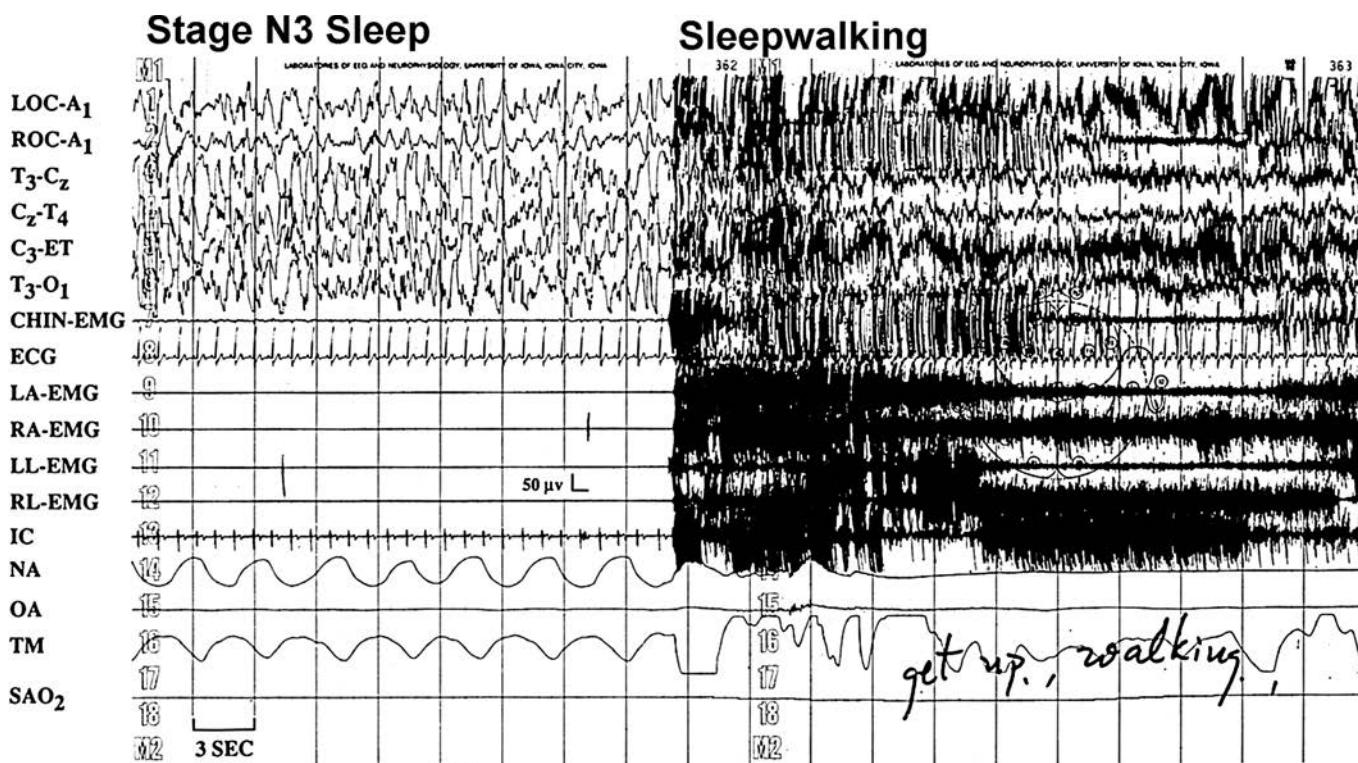
The normal atonia, or relative paralysis (paresis) associated with stage R (or dreaming) sleep, inhibits patients from fully physically acting out their dreams. This paresis is the result of active "REM sleep-on" cells in the midbrain that project caudally to stimulate periforniculus coeruleus centers in the brainstem, leading through a circuitous route to an inhibition of alpha motor neurons in the spinal cord and resulting in atonia.<sup>16</sup> In Parkinson's disease, degeneration of this descending tract in the periforniculus coeruleus area (defined as the sublateraldorsal nucleus in rats, the subcoeruleus area in cats, and undefined to date in humans) has been used to explain RBD (Fig. 15-8).<sup>17</sup>

There are three RBD subclassifications: subclinical (preclinical) RBD, the parasomnia overlap disorder, and status dissociatus.<sup>1</sup> Patients with subclinical RBD have a PSG that shows RWA, but they do not clinically have RBD (violent nocturnal behaviors). Nevertheless, at least 25% of these individuals will develop RBD. The parasomnia overlap syndrome is defined by a combination of RBD with one of the disorders of arousal

(confusional arousals, sleepwalking, or sleep terrors). Finally, the diagnosis of status dissociatus is always associated with another significant medical condition (possibly end-stage Parkinson's disease) and the inability to identify any PSG patterns suggesting a normal sleep stage.

**Case No. 1:** An elderly man complained of a long history of violent dreams associated with injurious behavior.<sup>18</sup> His wife also reported that he frequently "flops" his legs when he sleeps. Recently, he had a dream where he attempted to stop a man who was running from the police. Immediately prior to a full arousal, his spouse watched him jump head first off their bed (isomorphism). After another similar dream-related episode, he sustained superficial injuries to his face. In addition, a magnetic resonance imaging (MRI) scan of his brain revealed a right subdural hematoma.

PSG, with split-screen EEG-video analysis, showed significant PLMS (with a movement index of 52.0 events/h), and abnormally elevated muscle tone in stage R sleep. In stage R sleep, the patient abruptly began having running-like movements, after which he awoke and reported that he had just had a dream where he was "chasing cattle." His RBD resolved after taking clonazepam. Within 8 years, he developed PD with dementia, after which the patient subsequently died in a care facility.



**Figure 15-6.** This is the PSG tracing of a young woman experiencing a classic sleepwalking episode from stage N3 sleep (see the technician's note, "get up walking"). (A, left ear; C, central; ECG, electrocardiogram; EMG, electromyogram; ET, ears tied; IC, intercostal EMG; LOC, left outer canthus; LA, left arm; LL, left leg; NA, nasal airflow; O, occipital; OA, oral airflow; RA, right arm; RL, right leg; ROC, right outer canthus; SAO<sub>2</sub>, oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377-390; Fig. 14, with permission.)

**RECURRENT ISOLATED SLEEP PARALYSIS.** Recurrent isolated sleep paralysis, referred to by some using the Japanese term *kanashibari*, can occur at sleep onset (hypnagogic) or upon waking from (hypnopompic) sleep.<sup>1</sup> These are waking events that can last from seconds to minutes and are associated with the relative inability to move, during which up to 75% of patients may report associated active hallucinations.

The mean age of onset is 14 to 17 years, with a prevalence of at least one sleep paralytic spell that ranges from 5% to 40%.<sup>1,18,19</sup> Sleep paralysis may be precipitated by sleep deprivation and the supine sleeping position, and there may be a greater association with the use of anxiolytics, paranoia and bipolar affective disorder, and sleep-related cramps. The PSG may show elements of stage R sleep (REM-related atonia) and wakefulness (the intrusion of waking alpha waveforms into stage R sleep; Fig. 15-9).<sup>20</sup>

**Case No. 1:** During a formal PSG study, in REM sleep, a 47-year-old woman abruptly called out for help (Fig. 15-10).<sup>4</sup> Upon questioning, the patient was able to answer all the queries accurately. She indicated to the technologist that she could not move, but did so in a very dysarthric fashion secondary to relative facial paresis.

**NIGHTMARE DISORDER.** This disorder is associated with recurrent disturbing dreams (usually fearful and anxiety provoking) from stage R sleep that result in awakening followed by immediate dream recall.<sup>1</sup> Up to 50% of all children over 3 years

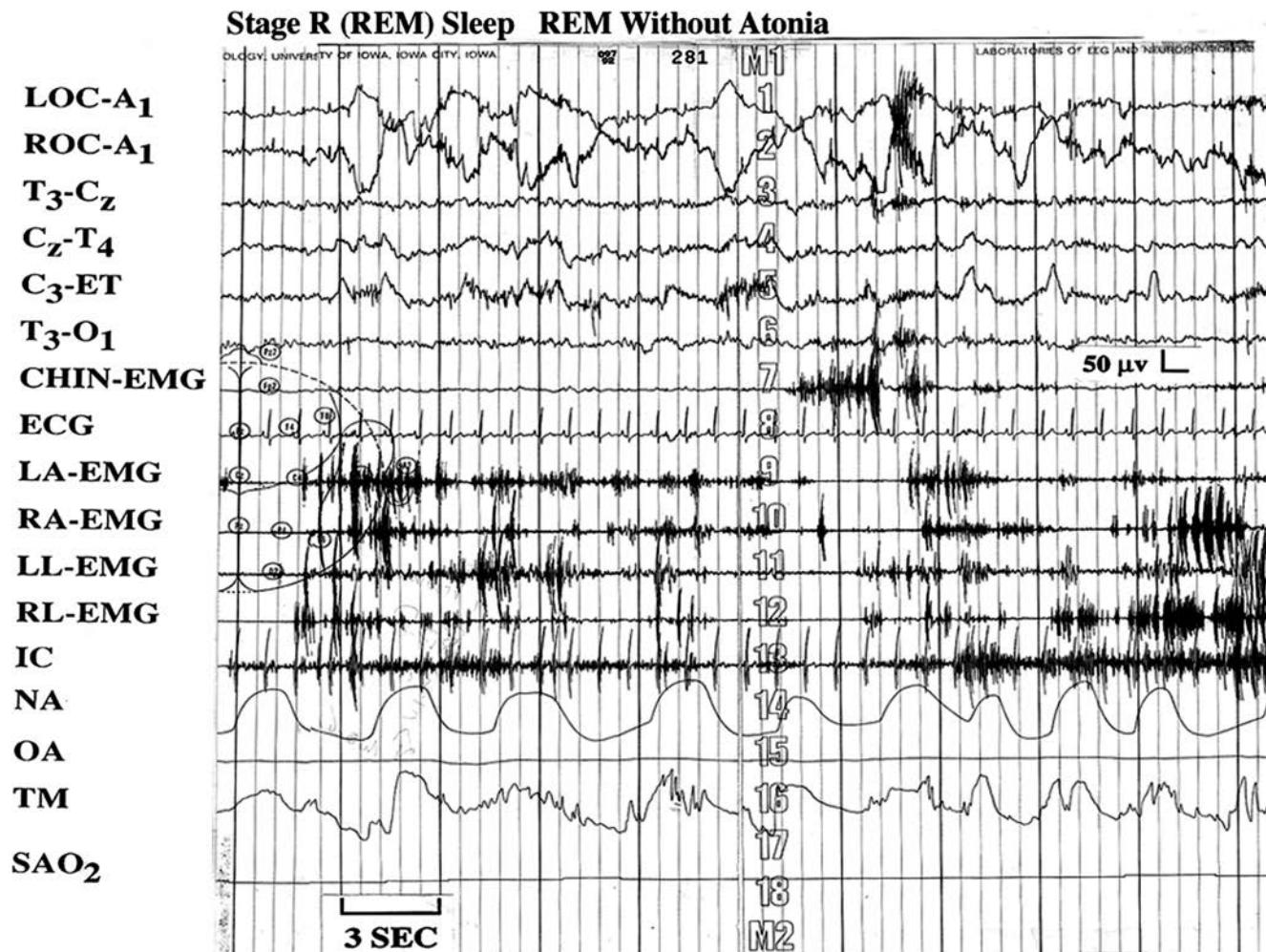
of age have a severe nightmare (up to 75% of the general population can recall at least one childhood nightmare). Nightmares usually begin between 3 to 6 years of age and peak at 6 to 10 years. Up to 8% of the general population has active nightmares (85% of adults report occasional nightmares).

Patients with acute stress and post-traumatic stress disorders are at increased risk for frequent nightmares.<sup>21</sup> In addition, the use of noradrenergics, serotonergics, gamma-aminobutyric acid (GABA), cholinergic and histaminergic drugs, and withdrawal from agents that suppress stage R sleep can exacerbate or precipitate nightmares.<sup>22</sup> The PSG generally reveals stage R sleep during a nightmare, at which time there is generally an elevation of autonomic activity evidenced as increased breathing and heart rates.

### Other Parasomnias

**SLEEP-RELATED DISSOCIATIVE DISORDERS.** The *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, defines a dissociative disorder as "...a disruption in the usually integrated functions of consciousness, memory, identity, or perception of the environment."<sup>23</sup> There are three categories of nocturnal dissociative disorders: dissociative identity disorder (multiple personality disorder), dissociative fugue, and dissociative disorder not otherwise specified.<sup>1</sup>

Patients with sleep-related dissociative disorders frequently have histories of physical or sexual abuse.<sup>1</sup> It predominates in



**Figure 15-7.** PSG tracings from the study of an elderly male with RBD clearly shows an unusual elevation of EMG activity during a prolonged period of stage R sleep [REM without atonia (RWA)]. This period was followed by an episode of violent behavior and an arousal, after which the patient immediately reported a dream that approximated his observed actions (isomorphism). (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Fig. 17, with permission.)

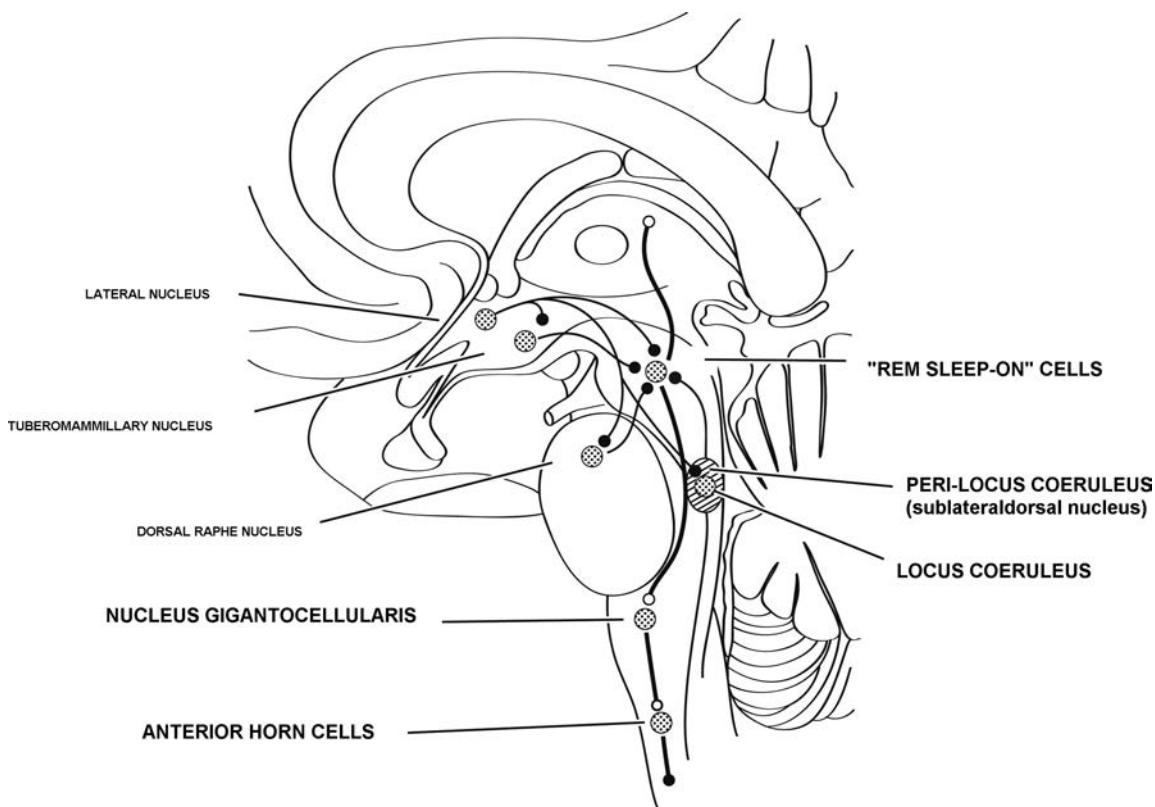
females with an onset that ranges from childhood to middle adulthood. Most patients with a sleep-related dissociative disorder suffer from a similar dissociative disorder during the daytime.

The patients suffer from dissociative behaviors from sleep, of which they are amnestic. These spells can last from minutes to over an hour, during which the patient often re-enacts a previous abuse, at which time injuries can occur.<sup>24</sup> After an arousal from sleep, up to a minute may pass before the patient demonstrates the dissociative behavior. During the spell, a waking PSG pattern has been reported.<sup>1</sup>

**SLEEP ENURESIS.** Sleep enuresis is recurrent involuntary urination/micturition during sleep (bedwetting) at least twice a week, in patients over 5 years of age.<sup>1</sup> It results from a mismatch between bladder capacity and urine volume, with an absent arousal response to a full bladder during sleep. There are two types of sleep enuresis: primary, where the patient has never been “dry” for 6 consecutive months, and secondary, where an individual, previously dry for 6 months, begins wetting at least two times a week for at least 3 months.

In infancy, voiding is a spinal reflex until approximately 18 months, after which voluntary control is first achieved during wakefulness, and later in sleep.<sup>1</sup> Maturational control is quite variable, and in otherwise normal patients primary enuresis occurs in 30% of 4 year olds, 10% of 6 year olds, 5% of 10 year olds, and in up to 2% of 18 year olds. Primary sleep enuresis is more common in boys than girls by a ratio of 3:2.<sup>1</sup> The prevalence of primary enuresis is 77% when both parents were enuretic and 44% if only one parent had childhood primary enuresis. There is a possible genetic linkage with primary enuresis to chromosomes 22q, 13q, and 12q. A rare cause of primary enuresis is a lack of normal sleep-related vasopressin (an antidiuretic hormone) release with subsequent high urinary volumes that exceed bladder capacity.

Secondary sleep enuresis can occur at any age. It can be seen in children with recent psychosocial stressors, and in adults with diabetes, urinary tract infections, nocturnal seizures, heart failure, obstructive sleep apnea (OSA), and dementia. PSG is only indicated in the assessment of secondary sleep enuresis when there is clinical suspicion of an additional primary sleep disorder such as OSA or sleep-related epilepsy.



**Figure 15-8.** This parasagittal section of the brain and brainstem shows the suspected pathology explaining RBD. In normal stage R sleep, “REM sleep on” cells in the midbrain pedunculopontine/lateral dorsal tegmental nuclear complex stimulate the nucleus gigantocellularis, which then hyperpolarize anterior horn cells in the spinal cord, subsequently leading to atonia/paresis. In RBD, degeneration in the peri locus coeruleus area (defined as the sublateraldorsal nucleus in rats, the subcoeruleus area in cats, and presently undefined in humans) has been postulated to disrupt descending tracts that would normally lead to atonia/paresis, thus allowing violent behaviors during stage R (dreaming) sleep. (*Open circle*, neurons normally activated during stage R sleep; *closed circle*, neurons normally inactivated during stage R sleep.) (Modified from Dyken ME, Yamada T. Narcolepsy and disorders of excessive somnolence. In: Ballard RD, Lee-Chiong TL Jr, eds. *Primary care: clinics in office practice*. Elsevier Saunders, 2005:389–413; Fig. 1, with permission.)

**SLEEP-RELATED GROANING (CATATHRENIA).** Catathrenia is expiratory sleep-related groaning that occurs following a deep inspiration, usually in the later stage R sleep periods.<sup>1,25</sup> It is a rare problem that may be more common in men, with 19 years reported as a mean age of onset. Although it is not associated with any medical, psychological, neurological, or upper airway anatomic abnormalities, catathrenia can disrupt the sleep of a bed partner, and on occasion has been associated with insomnia, daytime fatigue, and hoarseness.

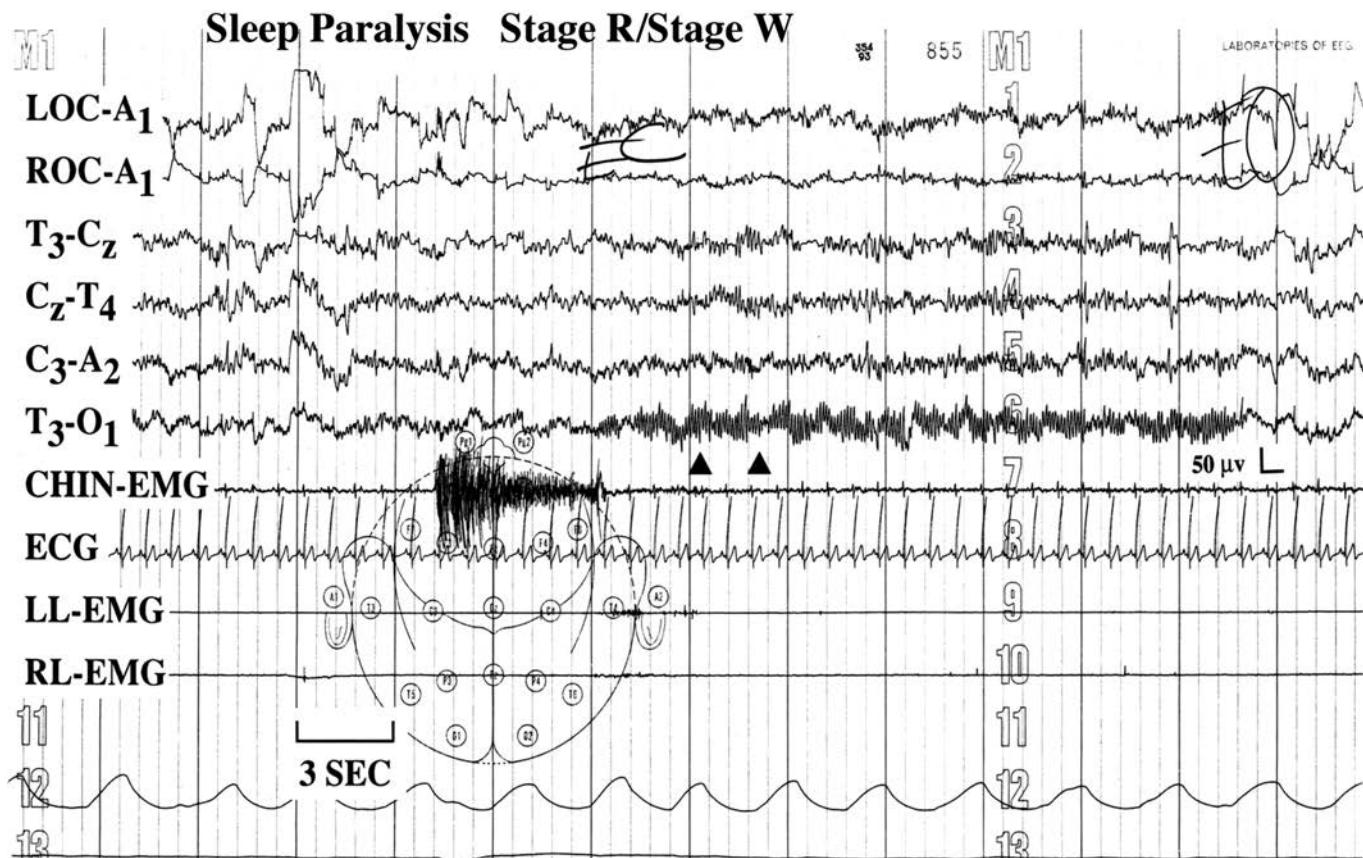
PSG studies have shown sustained groans (lasting 2 to 49 seconds) with repeat in clusters over a 2- to 60-minute period.<sup>1</sup> Groaning occurs only during the expiratory phase of a bradypnea (sometimes confused with central apnea) during which there is a slight decrease in heart rate and blood pressure and a moderate increase in intraesophageal pressure. The groan ends in a grunt or sigh, and is followed by a rebound increase in heart rate and blood pressure.

**EXPLODING HEAD SYNDROME.** This syndrome is associated with a sudden and frightening imagined loud noise or sense of explosion in the head as one is falling asleep or waking up.<sup>1</sup> It is more common in women (median age of onset of 58 years) and in stress. They are benign and resolve over years, although on occasion they can lead to insomnia.

The sensations occur most frequently during drowsiness and may be a sensory variant of a “sleep start” (hypnic jerks) as both occur during the transition from wake to sleep, and may occur with a visual hallucination (often a flash of light) and a brief myoclonic jerk.<sup>1</sup> On PSG, these events occur in early drowsiness with a relatively predominant alpha background activity, interspersed with theta waveforms and slow rolling eye movements.<sup>1,26</sup>

**SLEEP-RELATED HALLUCINATIONS.** These are usually visual in nature and occur at sleep onset (hypnagogic) and occasionally upon awakening (hypnopompic).<sup>1</sup> They can occur either with sleep paralysis or injurious behaviors during a particularly frightful hallucination. This disorder is more common in adolescents and young adults, and females, with a prevalence of up to 37% for hypnagogic hallucinations and up to 13% for hypnopompic events.

**SLEEP-RELATED EATING DISORDER.** The sleep-related eating disorder (SRED) occurs when amnestic involuntary repetitive episodes of involuntary eating and drinking from sleep lead to negative outcomes, such as obesity or the consumption of toxins.<sup>1</sup> These events can occur nightly and in any sleep stage. Typically, the patients eat high caloric foods (despite not being hungry) that they normally would not find desirable.



**Figure 15-9.** During a sleep paralytic event, this patient was asked to close the eyes (see the technician's notes; EC, eye closure; EO, eyes opening), at which time an 8 to 13 Hz alpha waveform (see the double arrowheads), a pattern typical for a relaxed waking adult with eyes closed, became superimposed over an underlying stage R (REM) sleep PSG pattern. [Stage R, stage R (REM) sleep; Stage W, awake]. (Modified from Dyken ME, et al. REM alpha rhythm: diagnostic for narcolepsy? *J Clin Neurophysiol* 2006;34:254–257; Fig. 1, with permission.)

SRED has a mean age of onset ranging from 22 to 29 years.<sup>1</sup> Women are primarily affected (83% of the patient population) and over 50% have had a previous parasomnia, such as sleep-walking or a sleep-related dissociative disorder.<sup>27</sup> SRED can also occur with restless legs syndrome, periodic limb movement disorder, OSA, circadian rhythm disorders, and narcolepsy. It has been precipitated by the use of zolpidem, triazolam, lithium carbonate, and anticholinergics, and during substance withdrawal.<sup>28</sup> SRED has also occurred in association with dieting and daytime eating disorders, stress, autoimmune hepatitis, and encephalitis.

Eighty percent of PSG studies will capture either confusional arousals or the nocturnal events of concern that are associated with eating.<sup>29</sup> SRED can arise from any sleep stage, after which a waking PSG is seen in association with a variable level of consciousness (Fig. 15-11).

**PARASOMNIA, UNSPECIFIED.** This diagnosis is given when the patient has symptoms that do not clearly fit the criteria to satisfy the classification for another standard parasomnia. Clinically, an underlying undiagnosed psychiatric condition is usually suspected.<sup>1</sup>

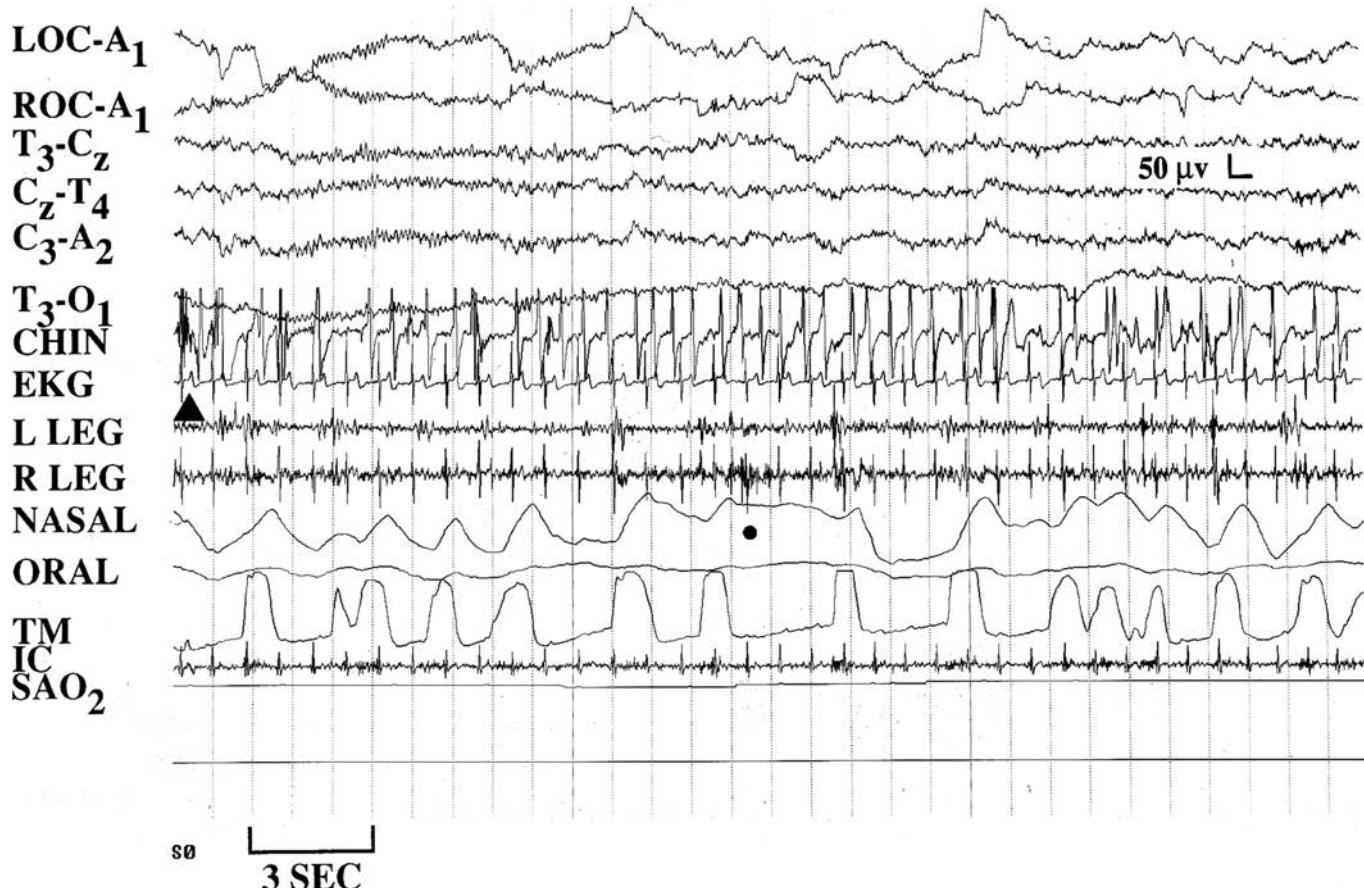
**PARASOMNIAS DUE TO DRUG OR SUBSTANCE.** This parasomnia, the direct result of consuming a substance, is

usually evidenced as a disorder of arousal (confusional arousal, sleepwalking, sleep terror), RBD, or the SRED. RBD has been reported with chocolate abuse, and the use of caffeine, selective serotonin reuptake inhibitors, venlafaxine (a serotonin-norepinephrine reuptake inhibitor), tricyclic antidepressants, monoamine oxidase inhibitors (such as selegiline), mirtazapine (a noradrenergic and specific serotonergic antidepressant), meprobamate, and anticholinesterase inhibitors, or during withdrawal from alcohol, amphetamines, barbiturates, and cocaine. RBD, sleep-related hallucinations, and nightmares can occur with  $\beta$ -adrenergic blocking agents such as bisopropiologol.<sup>1</sup>

**PARASOMNIAS DUE TO MEDICAL CONDITION.** This parasomnia is suspected to occur secondary to a concurrent medical or neurological condition. Symptomatic RBD secondary to Parkinson's disease is a classic example of such a parasomnia.<sup>1</sup> Oneirism (dream enactment during "wakeful dreaming") has been reported in fatal familial insomnia, Mangan's chorea, and in delirium tremens as part of a syndrome known as *agrypnia (insomnia) excitata*.<sup>30</sup> In agrypnia excitata, oneirism occurs in association with severe insomnia, confusion, and activation of motor and autonomic systems.<sup>1</sup>

Finally, complex nocturnal sleep-related hypnagogic and hypnopompic visual hallucinations can be seen in narcolepsy,

## Sleep Paralysis Stage R (REM) Sleep



**Figure 15-10.** During this sleep paralytic event, a woman suddenly called for help from stage R (REM) sleep (as indicated by the single arrowhead). When the technician asked her if she was all right, she responded “yeah” (indicated by the increase muscle tone immediately above the darkened circle). The patient reported that she could not move and that she had experienced a dream immediately prior to this event. ( $A_1$ , left ear;  $A_2$ , right ear; C, central; CHIN, chin electromyogram; EKG, electrocardiogram; IC, intercostal; L Leg, left leg EMG; LOC, left outer canthus; NASAL, nasal airflow; O, occipital; ORAL, oral airflow; R Leg, right leg EMG; ROC, right outer canthus;  $SAO_2$ , oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Fig. 16, with permission.)

Parkinson’s disease, dementia with Lewy bodies, peduncular hallucinosis, and in patients with loss of vision due to damage to the eyes or optic pathways (Charles Bonnet syndrome).<sup>1,31</sup> In some cases of degenerative disease, stroke, and brain injury, these hallucinations might result from a dysfunction of the reticular activating system due to damage to the serotonergic dorsal raphe nucleus of the brainstem, which could lead to a disinhibition of visual pathways that lead to the thalamic lateral geniculate nucleus.<sup>31</sup>

### THE DIFFERENTIAL DIAGNOSIS

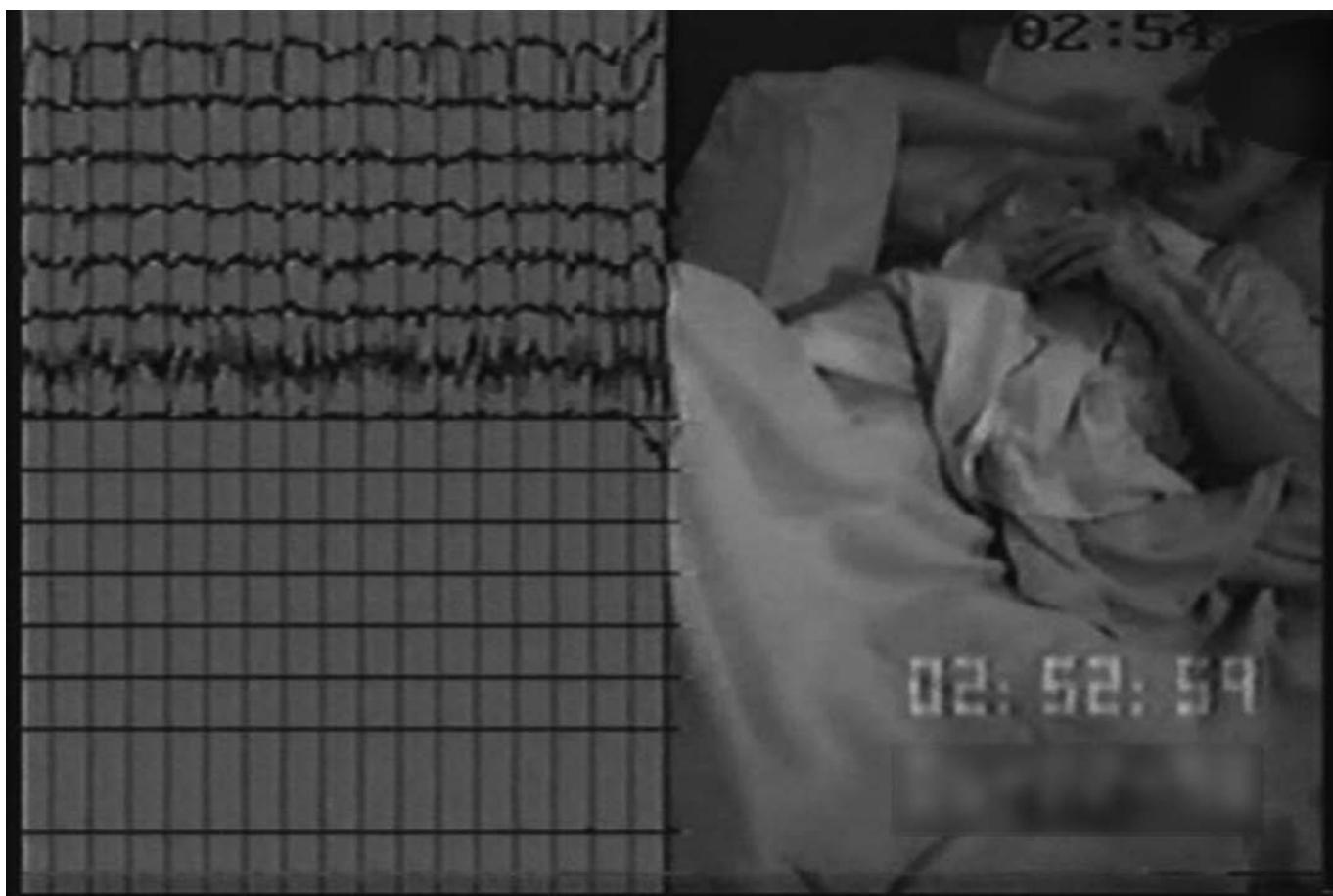
Included in the differential diagnosis of many parasomnias are nocturnal seizures and a variety of problems associated with significant sleep-related movements. In Appendix A of the ICSD, the classification of “Sleep-Related Epilepsy” is formally included under “Sleep Disorders Associated with Conditions Classifiable

Elsewhere.” Additional disorders that might suggest a parasomnia are classified in the ICSD under “Sleep-Related Movement Disorders” and include “Sleep-Related Bruxism” and “Sleep-Related Rhythmic Movement Disorder.”<sup>1</sup>

### SLEEP-RELATED EPILEPSY

The behaviors and movements associated with some nocturnal seizures can on occasion approximate a parasomnia (especially the disorders of arousals and RBD). In some instances, a sleep-related epilepsy may also be precipitated or exacerbated by another primary sleep disorder such as OSA. Formally, for a seizure disorder to be considered a “sleep-related epilepsy,” greater than 70% of seizures must occur during sleep.<sup>1</sup>

**Case No. 1:** A 10-year-old girl under many psychosocial stresses presented with nocturnal spells where she would awaken from sleep screaming and thrashing for very brief periods, after which she would quickly return to sleep.<sup>4</sup> Overnight continuous



**Figure 15-11.** This is a young man who presented for evaluation of possible sleep-related eating disorder. He reported repeatedly awakening in the morning with evidence of having eaten during episodes of which he was amnestic. During this event, he was eating graham crackers and chocolate bars, after which he drank a can of caffeinated cola. EEG showed awake record but the patient did not recall the event after he woke up in the morning.

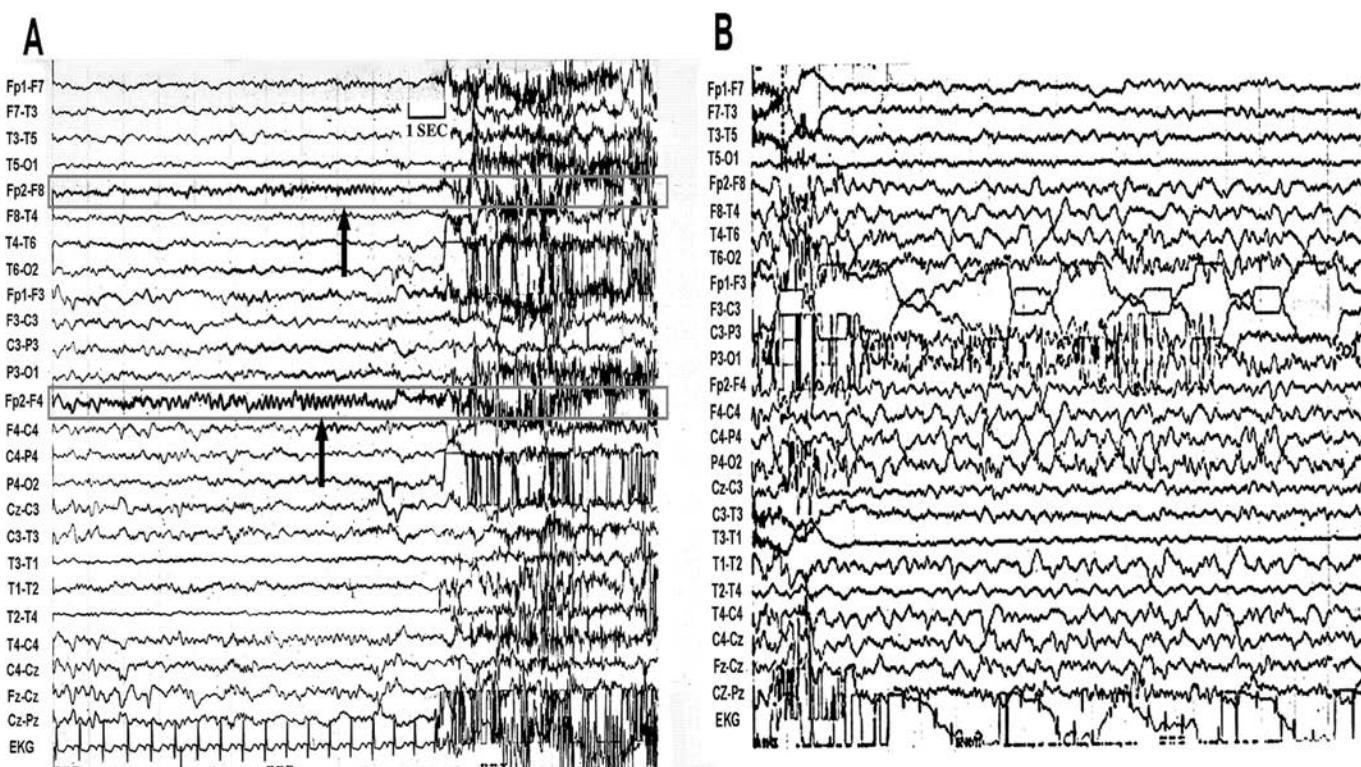
video-EEG monitoring captured 40 of her stereotypical nocturnal spells where she would abruptly arise in apparent fear and call out for her father, after which she would quickly return to her baseline level of waking mentation and then go back to sleep. Thirty-nine events arose from stage N2 sleep, while one came from stage R sleep. Although obvious EEG abnormalities were not appreciated during most spells, one event was associated with rhythmic, right frontal theta EEG activity, while another was followed by right hemispheric delta slow wave activity (Fig. 15-12). The clinical nature of the spells and the EEG findings suggested the diagnosis of nocturnal frontal lobe epilepsy (NFLE).

NFLE is associated with seizures that occur exclusively or predominately during sleep.<sup>32</sup> NFLE can present similarly to a disorder of arousal, including confusional arousals, sleepwalking, or sleep terror-like events.<sup>32,33</sup> NFLE can be mistaken for sleep terrors as these seizures frequently occur with elevated motor and autonomic activity, frequently with emotional vocalizations.

The EEG is often unremarkable; 55% of patients have normal interictal waking studies and 44% can have normal ictal PSG studies.<sup>32</sup> Patients with a deep-seated frontal lobe seizure focus might not have an abnormal EEG as 10 to 20 cm<sup>2</sup> of a synchronously activated gyral cortex is needed for surface scalp electrode EEG detection of spike activity.<sup>34</sup> In one study, the use of carbamazepine resulted in resolution of seizures in 20% of patients, with a reduction of seizure activity by at least 50% in another 48% of the individuals with NFLE.<sup>32</sup>

**Case No. 2:** An 8-year-old girl reportedly had sleep-related spells since age 2 years when she would suddenly arise, appear not to breathe, and demonstrate rocking movements. This would be followed by unresponsiveness, then confusion.<sup>4</sup> When under stress, the patient was prone to having confused nocturnal wanderings for which she was amnestic.

There was a family history of sleep walking and after two normal EEG studies and an unsuccessful anticonvulsant trial, a split-screen video-PSG was performed. Eight stereotypical



**Figure 15-12.** In this young patient with NFLE, only one of 40 clinical seizures associated with right frontal rhythmic theta activity, and only one spell was associated with postictal slowing from the right hemisphere. At the onset of seizure, EEG revealed right frontal rhythmic theta activity as outlined by the gray boxes (A). EEG showed right hemispheric delta activity immediately following a clinical seizure (B). (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Figs. 7 and 8, with permission.)

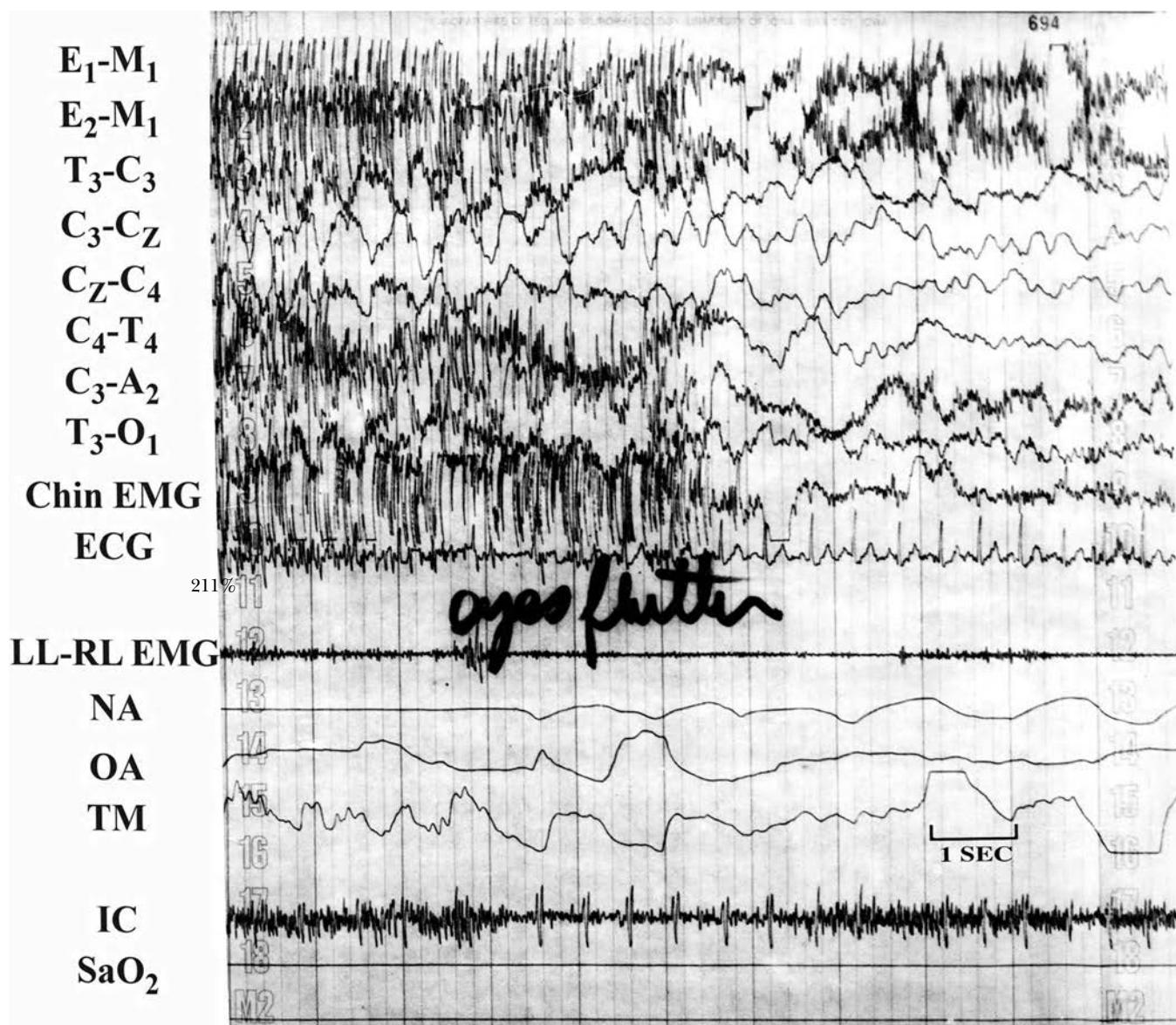
events were captured; one from stage N3 sleep, seven from stage N2 sleep. During these spells, she would suddenly sit up, become apneic while hyperextending her neck and right upper extremity. This was followed by generalized clonic activity, then loud, labored breathing, postictal confusion, and finally a return to sleep. Significant movement artifact made the PSG difficult to read. As such, only one event was clearly associated with obvious abnormalities on EEG. This was evidenced as poorly organized, postictal delta slow wave activity (Fig. 15-13).

When using PSG to distinguish between a parasomnia and a nocturnal seizure, there can be significant confounding factors, which Dyken et al.<sup>4</sup> have referred as the *interference pattern*. Minimal EEG abnormalities have been associated with some seizure types; in fact, none are seen in up to 10% of partial complex seizures.<sup>35,37</sup> Also, the limited EEG montage of the standard PSG may not include the epileptic focus, while short-lived EEG ictal changes are often hidden by movement artifacts.<sup>4</sup>

**Case No. 3:** A 25-year-old man presented for digital, split-screen, video-PSG monitoring to more accurately assess his history of medically intractable nocturnal complex partial

seizures.<sup>4</sup> This study revealed severe OSA. In addition, the patient reported six subjective seizures during arousals from stage R sleep throughout the night (four in association with apneas). Nevertheless, at the routine PSG sweep speed (10 mm/s), no EEG abnormalities were appreciated during these spells (Fig. 15-14A). As such, a REM variant of a confusional arousal, precipitated by the hypoxemia/hypercarbia and autonomic instability induced by OSA, was initially considered as a diagnosis. However, upon further review, using the standard EEG sweep speed of 30 mm/s, 18 Hz, centrally prominent beta activity (compatible with electrographic seizure) was uncovered (Fig. 15-14B).

It has been reported that synchronized NREM sleep encourages seizures, whereas desynchronized stage R sleep discourages seizure occurrence.<sup>4,38</sup> In this case, the increased frequency of seizures in stage R sleep may have been an epiphenomenon of OSA. Stage R sleep is normally associated with hypotonia. Apneas are often worse in stage R sleep due to the negative effects of hypotonia on an otherwise hypercompliant oropharynx. In this case, it was speculated that the hypoxic, hypercarbic, and autonomic stresses associated with the apneas may have preferentially precipitated seizures



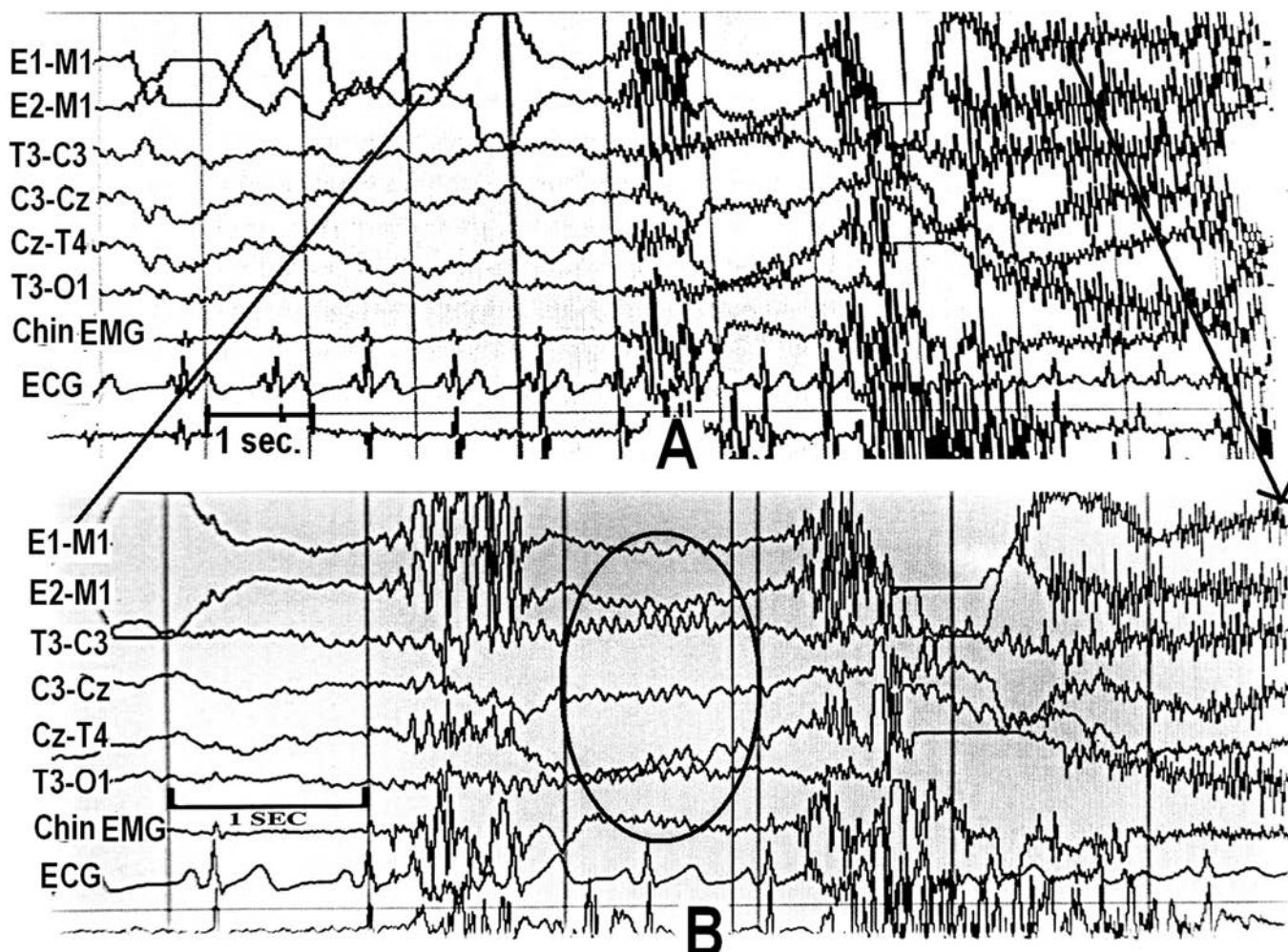
**Figure 15-13.** During the PSG of a young girl who had seven generalized tonic-clonic seizures from sleep, only one was associated with an obvious EEG abnormality that was appreciated as poorly organized postictal delta slow wave activity. (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377-390; Fig. 9, with permission.)

during stage R sleep, a stage of sleep otherwise considered relatively protective against seizure. It has been reported that treating sleep apnea may lead to improved seizure control in cases similar to this.<sup>38</sup>

#### SLEEP-RELATED MOVEMENT DISORDERS

**Case No. 1:** An 8-year-old girl was seen in prolonged rocking behaviors that often disrupted her sleep.<sup>4,39</sup> The patient's

mother reported that her daughter had frequent arousals where she would get up and "run around." In addition, she was often found in her bed humming and rocking, with the distinction between waking and sleep difficult to discern. Recently she had fallen out of bed on several occasions, after which relatively violent movements continued, resulting in superficial head injuries and epistaxis. The patient was also enuretic twice a week. In addition, she had a 6-year-old brother with similar rocking behaviors.



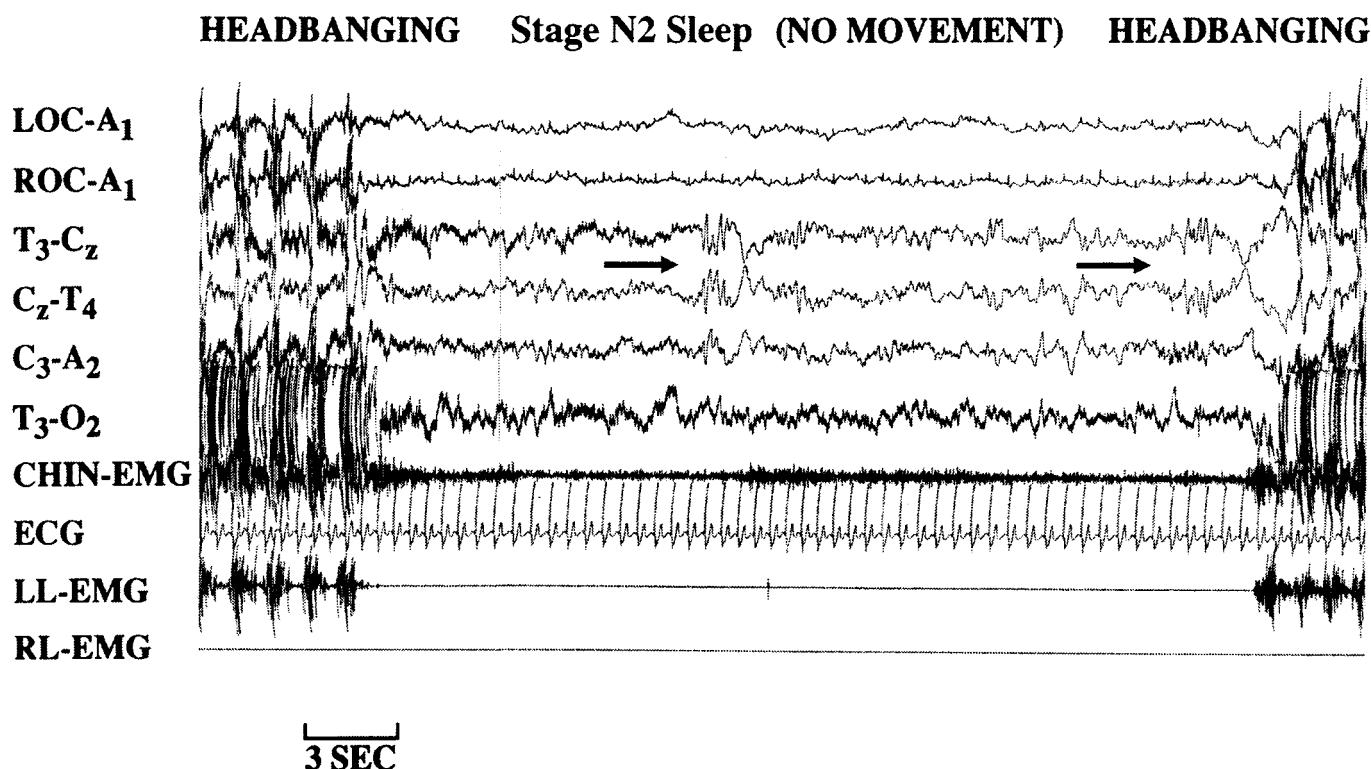
**Figure 15-14.** In a patient with suspected intractable sleep-related seizures, a PSG tracing at the standard sleep recording speed of 10 mm/s showed an obstructive apnea immediately preceding his arousal and report of having “another seizure,” although the EEG appeared to show no clear epileptiform activity contaminated by muscle or movement artifacts (A). When the same event was analyzed with a sweep speed of 30 mm/s, this allowed to reveal low-voltage beta activity indicating the onset of an electrographic seizure (shown by circle) (B). (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Fig. 11, with permission.)

Her examination showed small superficial injuries on the upper and lower extremities. An MRI of the brain was normal. A video-PSG revealed episodes of relatively violent body movements (evidenced as head banging and body rocking) that began abruptly from either stage N1 or N2 sleep (often in strong association with K-complexes), and were immediately followed by stage N1, N2, or stage R sleep on rare occasions. No epileptiform activity was seen.

The patient’s history and PSG analysis are classical for the rhythmic movement disorder (RMD) as classified in the ICSD.<sup>1</sup> In RMD, movements include body rocking, head banging, and head rolling and less commonly body rolling, leg banging, or

leg rolling, often in association with inarticulate rhythmic humming or oral sounds (Figs. 15-15 and 15-16).<sup>1</sup> RMD can occur in transitions to stage N1 sleep, but it is strongly associated with stage N2 sleep.<sup>39</sup>

Rhythmic body movements in drowsiness and sleep occur in 59% of 9-month-old infants, in 33% of all children at 18 months, and in 5% of 5-year-old children, and are only considered a formal sleep disorder if they significantly impair sleep or daytime functioning, or cause injury.<sup>1</sup> Most patients with RMD are normal, although in older children and adults there may be a greater association with intellectual disabilities (mental retardation) and autism.



**Figure 15-15.** Immediately after and before respective episodes of headbanging, the young girl with RMD stopped moving for a period of time, which allowed the recognition of stage N2 (NREM) sleep with characteristic K-complexes (as depicted by the two *black arrows*) with negative sharp waves followed by positive components (total duration lasting  $\geq 0.5$  seconds). (A<sub>1</sub>, left ear; A<sub>2</sub>, right ear; C, central; ECG, electrocardiogram; EMG, electromyogram; LOC, left outer canthus; LL, left leg; O, occipital; RL, right leg; ROC, right outer canthus; T, temporal.) (From in Dyken ME, et al. Diagnosing rhythmic movement disorder with video-polysomnography. *Pediatr Neurol* 1997;16:37-41; Fig. 1, with permission.)

### Sleep Bruxism

Sleep bruxism is stereotypic grinding movements of the teeth during sleep (nocturnal tooth grinding) often seen in normal children with a prevalence of up to 17%, and adults with a prevalence of up to 8%.<sup>1</sup> It can be divided into primary forms (without known cause, most often seen in healthy children and adults) and secondary forms [often seen in children with intellectual disabilities (mental retardation) and adults under stress].<sup>40</sup> Up to 50% of patients have a family member with a history of bruxism.

Bruxism is associated with two types of jaw contractions: tonic/isolated sustained contractions and rhythmic masticatory muscle activity (RMMA), which appear as a series of repetitive jaw clenches.<sup>1</sup> Excessive bruxism can lead to dental damage, temporal-mandibular injuries, facial pain, headaches, insomnia, and disruption of a bed partner's sleep.<sup>41,42</sup>

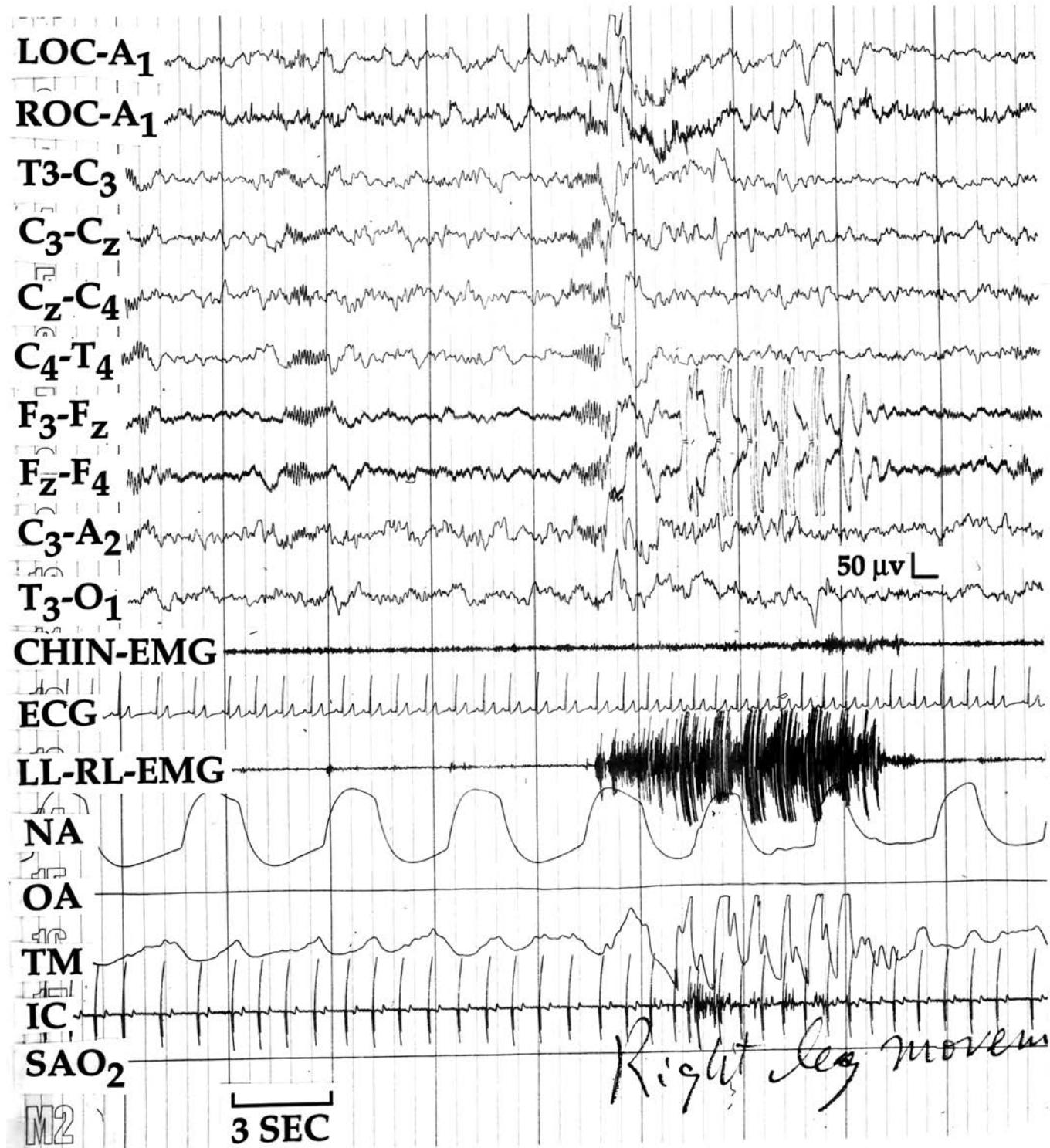
The ICSD states that for PSG diagnosis of bruxism a minimum of one masseter EMG monitoring electrode is required.<sup>1</sup> Tonic bruxism appears as sustained EMG activity greater than 2 seconds, while RMMA is recognized by phasic/repetitive periods of 1-Hz EMG activity lasting 0.25 to 2 seconds, with greater than 80% of the activity occurring in stage N1 and N2 sleep. The diagnosis demands at least four episodes of bruxism/h (or 25 individual muscle bursts/h) and at least two audible episodes of tooth grinding during the entire study.<sup>1</sup>

**Case No. 1:** A 23-year-old woman with significant stressors reported frequent nightmares associated with screaming arousals.<sup>4</sup> Her PSG showed significant bruxism with RMMA recognized as a pattern of rhythmic muscle artifact throughout multiple channels of the study. The conventional PSG sweep speed of 10 mm/s (or 30 seconds/page) relatively compressed the data making EEG-based sleep staging impossible (Fig. 15-17A). By digitally expanding the EEG, and utilizing the faster sweep speed of the conventional EEG study (30 mm/s, or 10 seconds/page) correlating the muscle activity of bruxism with a specific sleep state was possible (Fig. 15-17B).

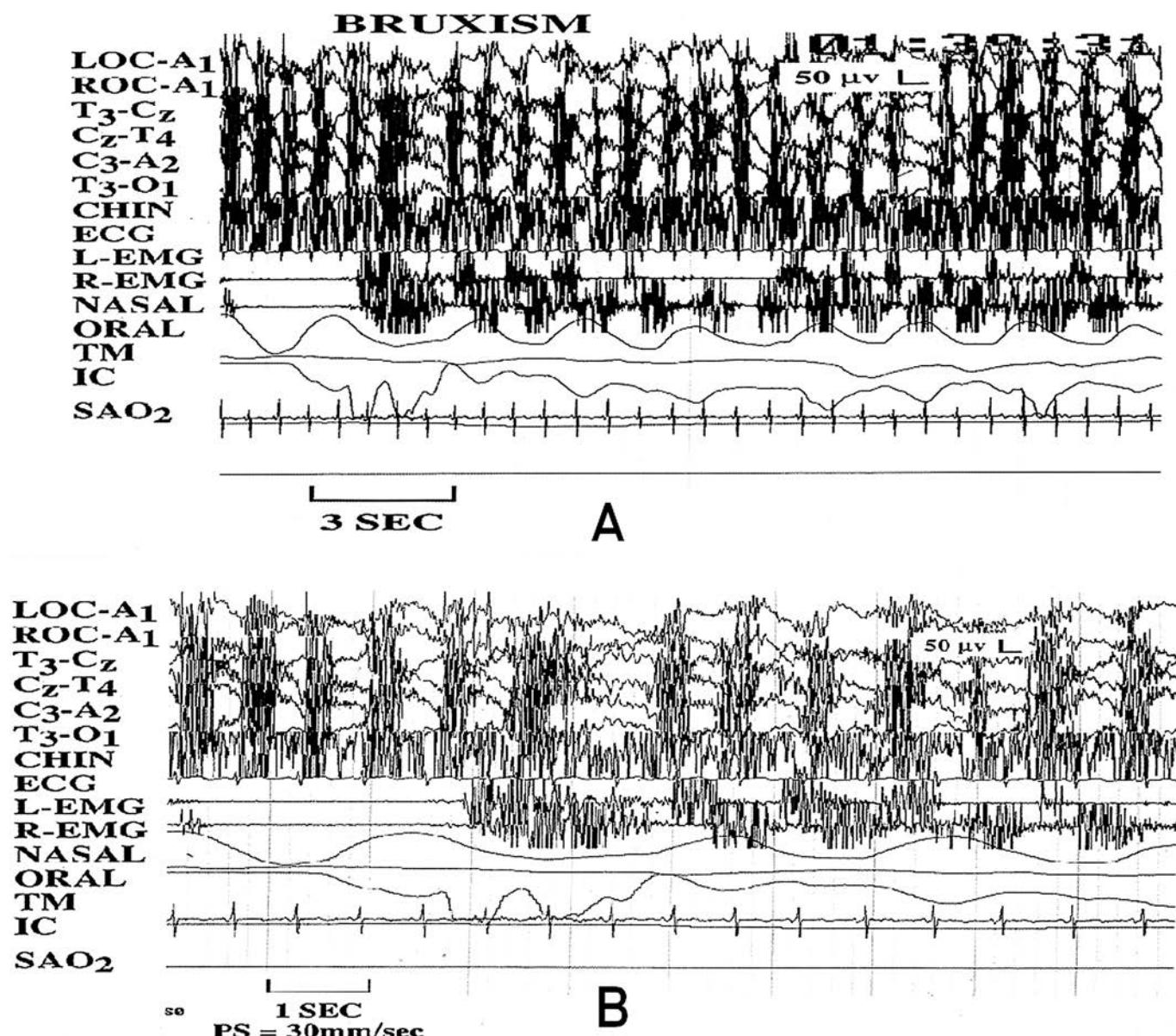
### SUMMARY

Parasomnias, sleep-related epilepsy, and sleep-related movement disorders can cause, complicate, or be the result of a variety of health-related problems. In addition, the clinical presentations of patients with any of these disorders can often be quite similar. As such, their successful differentiation and consequent treatment regimens can often be realized through the judicious use of PSG with prolonged split-screen video-EEG analysis. When an event of interest is captured in such a setting, the concomitant active clinical evaluation performed by the recording technician is invaluable.

## Stage N2 (NREM 2) Sleep Legbanging



**Figure 15-16.** PSG of a young boy with RMD shows isolated legbanging (see technologist's indicated right leg movement). The relatively minimal muscle artifact permitted a clear appreciation of sleep spindles and a possible K-complex in association with the onset of leg movements during stage N2 (NREM) sleep. (A<sub>1</sub>, left ear; A<sub>2</sub>, right ear; C, central; ECG, electrocardiogram; EMG, electromyogram; IC, intercostal; LOC, left outer canthus; LL-RL, left leg-right leg; NA, nasal airflow; O, occipital; OA, oral airflow; ROC, right outer canthus; SAO<sub>2</sub>, oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, et al. Diagnosing rhythmic movement disorder with video-polysomnography. *Pediatr Neurol* 1997;16:37-41; Fig. 3, with permission.)



**Figure 15-17.** Excessive muscle artifact from sleep bruxism made the electrical distinction between waking and sleep impossible while running the study at the routine PSG paper (sweep) speed of 10 mm/s (**A**). Digital expansion of the data from the bruxism depicted in **A** was analyzed at a paper speed of 30 mm/s in **B**. This allowed the recognition of underlying theta/delta slow activity of sleep. (A<sub>1</sub>, left ear; A<sub>2</sub>, right ear; C, central; ECG, electrocardiogram; EMG, electromyogram; IC, intercostal; LOC, left outer canthus; L, left leg; O, occipital; PS, paper speed; R, right leg; ROC, right outer canthus; SAO<sub>2</sub>, oxygen saturation; T, temporal; TM, thoracic movement.) (Modified from Dyken ME, Yamada T, Lin-Dyken DC. Polysomnographic assessment of spells in sleep: nocturnal seizures versus parasomnias. *Seminars Neurol* 2001;21:377–390; Figs. 19 and 20, with permission.)

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## SECTION V

# Nerve Conduction Studies

CHAPTER

## 16

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Sheila Mennen  
Leigha Rios

# Nerve Conduction Studies

### ABBREVIATIONS:

cm	Centimeter
CMAP	Compound muscle action potential
EMG	Electromyography
Hz	Hertz
mA	Millamps
ms	Millisecond
mV	Millivolt
µV	Microvolt
NCS	Nerve conduction studies
kHz	Kilohertz
SNAP	Sensory nerve action potential

### INTRODUCTION AND RECORDING TECHNOLOGY

Nerve conduction studies (NCS) have been around since the end of the 18th century. Early NCS were discovered by Galvani, who, at that time discovered that sending electrical signals through the nerves of animals elicited a muscle contraction.<sup>1</sup> This discovery led to the development of the diagnostic tool that is commonly used today as an aide in the diagnosis of numerous nerve and muscle disorders.

In the early years, NCS were recorded using the basic concepts of electricity and a device called the *capillary electrometer*. This was upgraded to the string galvanometer.<sup>1</sup> As NCS quickly gained acceptance, the equipment and techniques demanded improvement. In the 1920s, the development of the cathode ray oscilloscope<sup>1</sup> opened the door to the era of analog recording from which we have only recently (within the past 10 years) steered away. Analog recording used an oscilloscope to measure the electrical signals that were sent across the nerves. The stimulation produced a *compound muscle action potential* (CMAP) that appeared as a waveform on the oscilloscope. This allowed measurement of the latency, amplitude, and velocity of the waveform, giving vital information regarding the health of the nerves. The downside to analog technology is that a single response can never be duplicated.<sup>2</sup> This is when digital technology stepped in. Digital recording allows data manipulation after recording is completed, which in turn aids more accurate information and interpretation. Improved technology has also provided computerized calculations (quantitative analyses) that lead to a decrease in human errors.

### NCS TECHNIQUES

NCS is commonly used when a patient presents with neuropathic symptoms, such as pain, numbness, tingling, burning, or weakness that may be indicative of nerve damage. When performing a

**TABLE 16.1****Parameter Settings for NCS**

Study Type	Sensitivity	Hi Cut (kHz)	Low Cut (Hz)	Sweep (ms)	Stimulation Rate
Motor	5 mV	5	2	2	
Sensory	20 µV	2	20	1	
F-wave	500 µV	3	20	5	
H-reflex	500 µV	5	2	5	
Blink Reflex	500 µV	3	10	10	
Repetitive Nerve Stimulation	2 mV	5	2	5	3 Hz

basic NCS, there are two main types of studies, motor and sensory. When looking for a specific type of nerve injury, other types of NCS can be performed including F-waves, H-reflex, blink reflex, and repetitive nerve stimulation. Recording parameters must be set to obtain quality waveforms (Table 16.1). The waveforms are compared against normative data determined by each laboratory

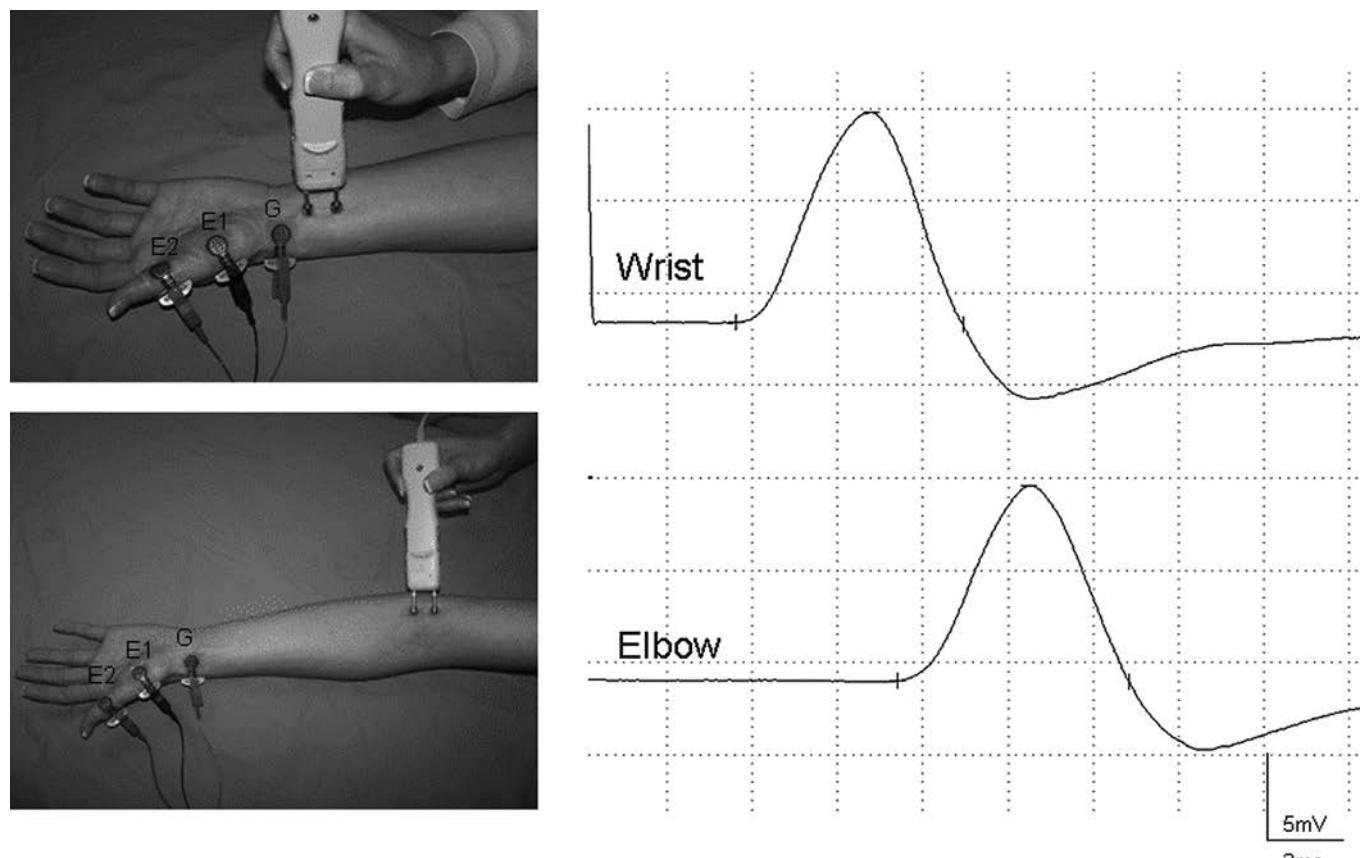
to define normal values. Various techniques may be used when performing NCS; however, the following techniques demonstrate our laboratory protocols.

### MOTOR STUDY

In a motor NCS, the active electrode (E1) is placed over the belly of a muscle supplied by the nerve being studied. The reference electrode (E2) is placed 3 to 4 cm distal to E1, preferably on a bony prominence, and the ground is placed in between the stimulating and the E1 electrodes. Stimulation of 0 to 100 mA (1–400 V) with a duration ranging from 0.1 to 1.0 ms is applied supramaximally to several points along the course of the nerve being studied. When stimulating the motor nerves, the cathode (–) should be placed toward the active electrode. Stimulation elicits a CMAP at each stimulation site that is measured and calculated. Each nerve has a specific set up (Table 16.2A). Figures 16-1 to 16-4 show examples of stimulation and recording sites for the median, ulnar, peroneal, and posterior tibial nerve.

**TABLE 16.2****Motor and Sensory Nerve Electrode Placement**

Nerve	Active Electrode (E1)	Reference Electrode (E2)	Ground	Stimulation site
<b>A. MOTOR NERVE</b>				
Median	Abductor Pollicis Brevis (APB)	Metacarpophalangeal joint of thumb	between the stimulating and recording electrodes	<p><i>Wrist</i> 2 cm proximal to the distal wrist crease between the flexor carpi radialis (FCR) and the palmaris longus (PL) tendons</p> <p><i>Elbow</i> at the elbow crease, medial to biceps tendon</p>
Ulnar	Adductor Digiti Minimi (ADM)	Proximal phalanx of the 5th digit	between the stimulating and recording electrodes	<p><i>Wrist</i> 2 cm proximal to the distal wrist crease, anterior to the flexor carpi ulnaris tendon</p> <p><i>Below Elbow</i> 2–4 cm distal to the medial epicondyle</p> <p><i>Above Elbow</i> 10 cm proximal to the below elbow site</p>
Peroneal	Extensor digitorum Brevis (EDB)	Base of the 5th metatarsal	between the stimulating and recording electrodes	<p><i>Ankle</i> 8 cm from E1 between EHL (extensor hallucis longus) and the EDL (extensor digitorum longus) tendons</p> <p><i>Below Fibular head</i> Posterior to the fibular head</p> <p><i>Above fibular head</i> Lateral third of popliteal crease</p>
Tibial	Adductor Hallucis Longus (AHL)	Distally near the 1st metatarsal	between the stimulating and the recording electrodes	<p><i>Ankle</i> Posterior to medial malleolus</p> <p><i>Knee</i> In the popliteal fossa slightly lateral to midline</p>
<b>B. SENSORY NERVE</b>				
Median	Proximal phalanx of the 2nd or 3rd digit	Distal phalanx of the 2nd or 3rd digit	between the stimulating and the recording electrodes	2 cm proximal to the distal wrist crease between the FCR and the PL tendons
Ulnar	Proximal phalanx of the 5th digit	Distal phalanx of the 2nd or 3rd digit	between the stimulating and the recording electrodes	2 cm proximal to the distal wrist crease, anterior to the flexor carpi ulnaris tendon
Sural	Posterior to the lateral malleolus	3–4 cm distal to E1	between the stimulating and recording electrodes	14 cm proximal to E1, on the posterior area of the leg



**Figure 16-1.** Median motor NCS performed with the E1 placed on the belly of the abductor pollicis brevis (APB), E2 placed 3 to 4 cm distal to E1 and the ground (G) placed in between the E1 and the stimulating electrodes. The pictures illustrate the proper stimulation sites at the wrist and the elbow. The stimulator polarity should be cathode (-) distal. The corresponding waveform provides an example of a normal CMAP elicited at that stimulation site.

## SENSORY STUDY

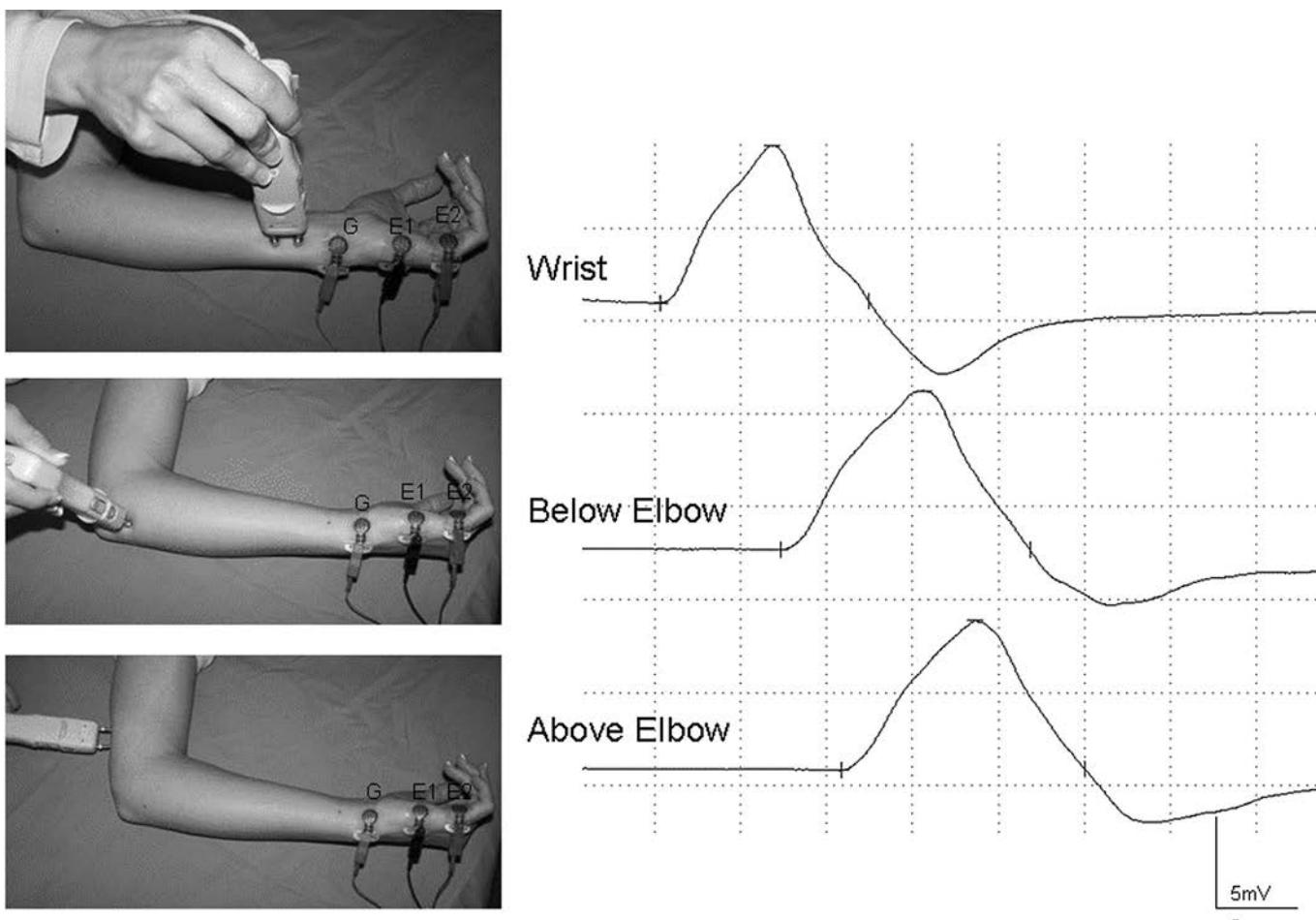
Sensory studies are performed similar to motor studies with a few major differences. In a sensory NCS, the E1 electrode is not placed over the belly of a muscle; rather, it is placed over another segment of the nerve. The reference is placed 3 to 4 cm distal to the E1 electrode and the ground is placed in between the stimulating and E1 electrodes. Stimulation of 0 to 100 mA (1–400 V) with a duration of 0.1 milliseconds may be applied supramaximally to either a single site or several points along the course of the nerve being studied. Similar to the motor nerve stimulation, the cathode (-) should be toward the active electrode. For sensory studies, the stimulation elicits a sensory nerve action potential (SNAP) at each stimulation site, which is then measured and calculated. One stimulation site is needed when calculating the conduction velocity of a sensory nerve due to the fact that the SNAP is being calculated from one site of the nerve to another. Like motor studies, the sensory nerves have a specific set up to record the nerve being studied (see Table 16.2B). Figures 16-5 to 16-7 show examples of recording electrode placement and stimulation sites for the median, ulnar, and sural sensory nerves.

## F WAVES

F waves are recognized as a useful tool in NCS and are frequently used as a part of the motor NCS to assess the entire

length of the nerve. The F wave sends the antidromic signal from the stimulation site up through the anterior horn cell producing a late response from the spinal cord. Evaluation of a longer nerve segment gives the physician valid information regarding axonal loss and demyelination along the entire length of the nerve. Information from a longer nerve segment is helpful when making an early diagnosis of a diffuse process, such as diabetic polyneuropathy or Guillain Barre syndrome. When testing a longer nerve segment and accumulating all the segmental changes, it is more likely to produce detectable abnormalities earlier in the disease process.

F waves can be recorded from any motor nerve being tested. The F wave is performed using the same electrode set up as the motor NCS. The difference occurs when the polarity of the stimulator is reversed. Unlike with motor and sensory nerves, when recording F waves, the anode (+) should be distal toward the active electrode. A train of at least 10 stimuli is applied supramaximally to the nerve being tested, eliciting an M wave, an A wave, and the F wave. The M wave is a direct motor response and the A wave (which is not always recorded) is an abnormal axonal response indicating chronic nerve injury. Both the M and A waves are consistent, reproducible waves forms. The F wave differs from these as they appear inconsistently and have varying latencies. When measuring the F wave, use the latency of the earliest F wave that is evoked for your measurements (Fig. 16-8).



**Figure 16-2.** Ulnar motor NCS performed with the E1 placed on the belly of the adductor digiti minimi (ADM), E2 placed 3 to 4 cm distal to E1, and the ground (G) placed in between the E1 and the stimulating electrodes. The pictures illustrate the proper stimulation sites at the wrist, below elbow, and above the elbow. The stimulator polarity should be cathode (–) distal. The corresponding waveform provides an example of a normal CMAP elicited at that stimulation site.

## H REFLEX

The H reflex is another study that is used in addition to routine NCS, most commonly when there is a question of S1 radiculopathy. The H reflex evaluates the S1 nerve root by sending submaximal stimulation up the group 1A afferent sensory fibers of the tibialis posterior nerve. These sensory fibers are elicited by delivering a low-intensity, high-duration stimulation, rather than the high-intensity, low-duration stimulation that produces a CMAP in a regular NCS.

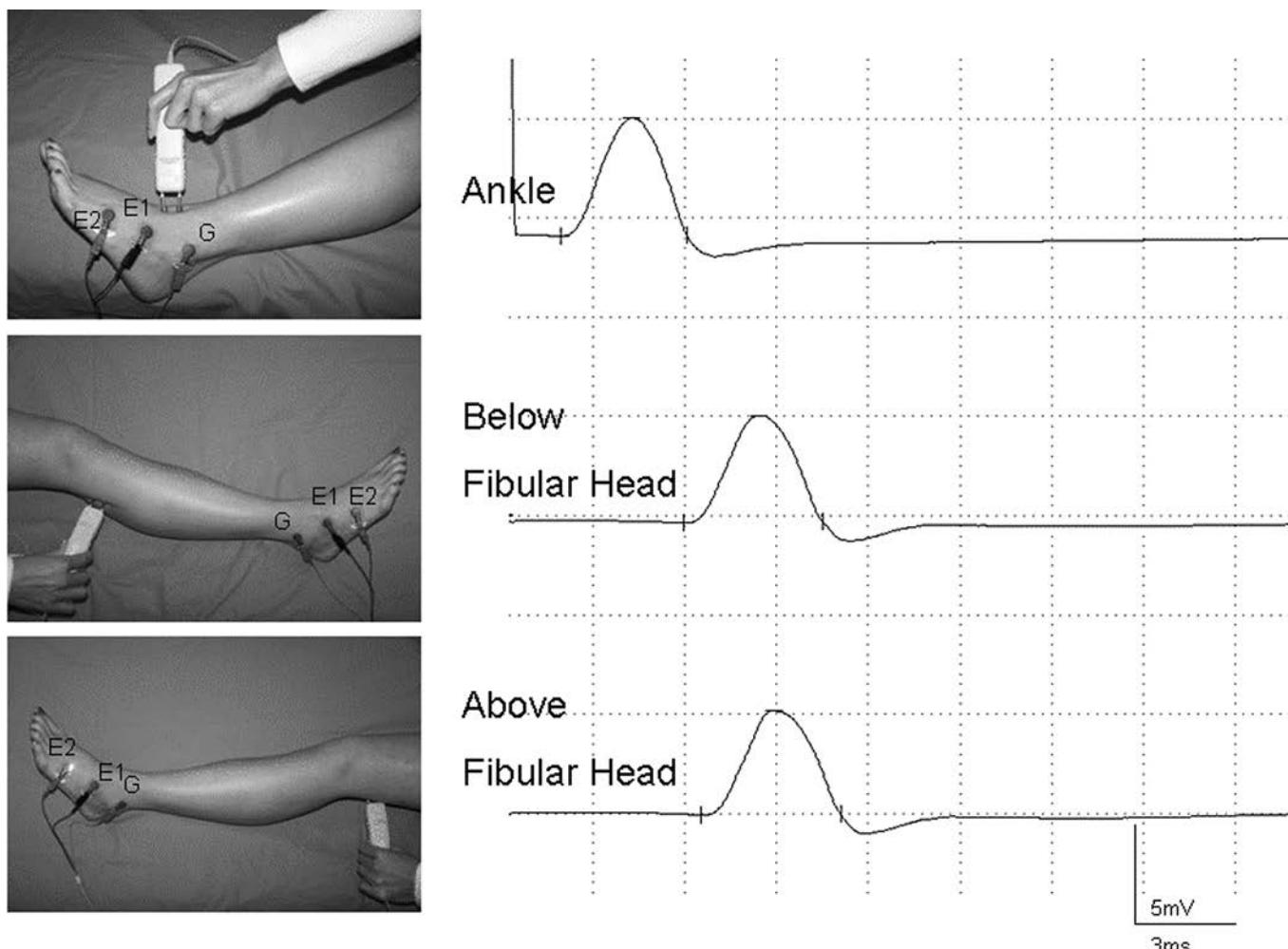
Set up for this study is consistent with a motor NCS, using the belly of the soleus muscle as the placement for the E1. When stimulating behind the knee (see Fig. 16-4), the polarity of the stimulator should be cathode (–) proximal, as done with the F wave. Stimulation of the H reflex elicits an M response and an H reflex. The H reflex will appear as a larger, more consistent, reproducible waveform than the M wave. When recording the H reflex, a stimulus duration of 1 ms should be used. As the stimulation intensity is increased, both the M and H waves will appear. Decreasing the intensity will then decrease the size of the M wave and evoke a recordable H reflex that is at least

twice the size of the M wave. If the amplitude of the M wave exceeds that of the late response, the waveform elicited is an F wave. This provides the physician with incorrect values regarding the S1 nerve root, which should be disregarded. The latency of the H reflex is most important and is usually compared side to side (Fig. 16-9).

## WAVEFORM ANALYSIS

When making a diagnosis based on NCS, many physicians depend on the technologist to make reliable decisions when reporting the findings. Learning how to properly measure and calculate the acquired waveform is key to providing the physician with accurate information. Mismarking and incorrect measuring of distances is one of the most common mistakes made by technologists.<sup>3</sup>

When marking a waveform, there are several points that need to be marked, each point being significant to a specific portion of the nerves' function. The size of the wave, or the



**Figure 16-3.** Peroneal motor NCS performed with the E1 placed on the belly of the extensor digitorum brevis (EDB), E2 placed 3 to 4 cm distal to E1, and the ground (G) placed in between the E1 and the stimulating electrodes. In this example, G has been placed on the lateral malleolus. The pictures illustrate the proper stimulation sites at the ankle, below and above the fibular head. The stimulator polarity should be cathode (–) distal. The corresponding waveform provides an example of a normal CMAP elicited at that stimulation site.

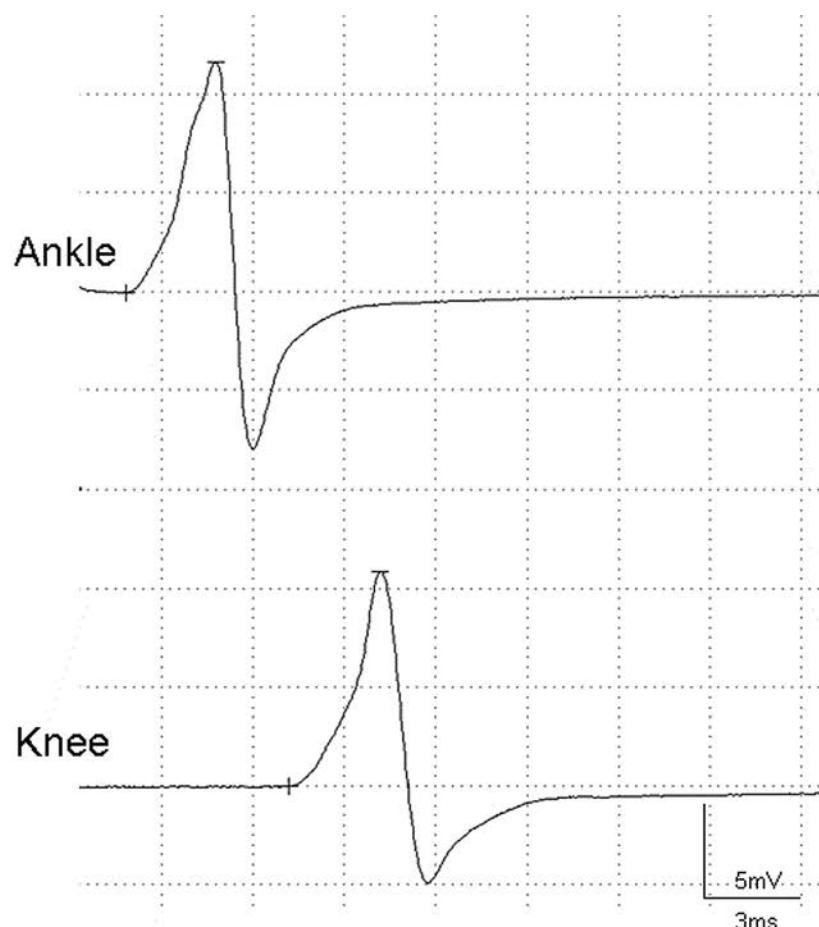
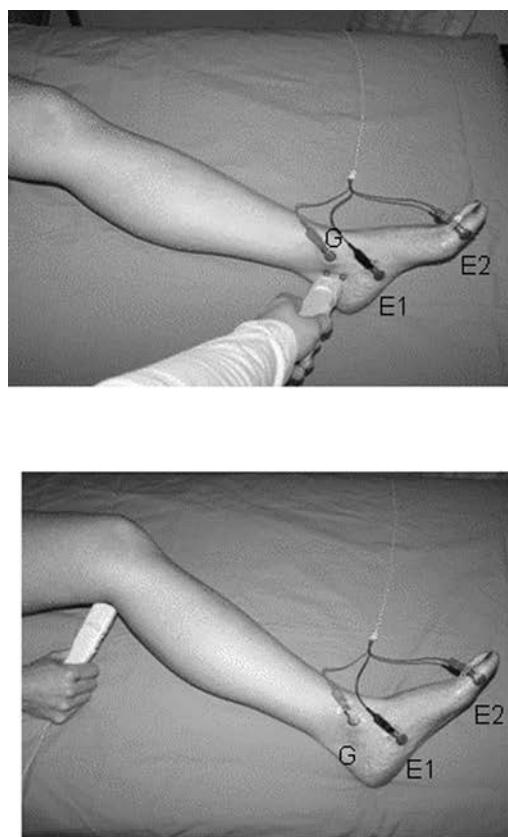
amplitude, is measured from the baseline to the peak of the waveform. This indicates how many of the nerves' axons are responding to the stimulation. In axonal neuropathy (neuropathy affecting mainly the axon leaving the myelin sheath mostly intact), the amplitude is depressed without significant change in latency. The onset latency reflects the time it takes the stimulation impulse to travel from the stimulation site to E1. The duration is the time it takes for the CMAP to return to baseline (this measurement is not used for sensory NCS) (Fig. 16-7). The final measurement is called the *nerve conduction velocity* (NCV) (Table 16.3A and B) and is calculated by using the distance between the stimulation sites divided by the latency difference. When calculating a motor NCV, two or more stimulation sites are needed, whereas a sensory NCV only requires one stimulation site. This is due to the fact that an NCV must be calculated using a nerve-to-nerve segment (Fig. 16-10). The latency, duration, and conduction velocity provide information regarding the health of the myelin sheath surrounding the nerve. In contrast, latency is mainly affected in demyelinating neuropathy but axonal neuropathy does not show much change in latency.

## UNCOMMON NCS TECHNIQUES

NCS aids in the diagnosis of numerous types of nerve disorders. Most nerve disorders are accessed by performing routine studies that consist of the median, ulnar, peroneal, posterior tibial and sural nerves. However, specific symptoms may indicate the need for more extensive nerve testing. Table 16.4A and B describe the techniques that are used for some of the additional nerves that may be requested.

## ARTIFACTS

When performing routine NCS, standard techniques are used to ensure an adequate study is achieved. However, at some point, even after appropriate measures have been taken, all technologists will experience difficulty acquiring waveforms. Artifacts generally fall under two different categories, electrical or physiological.<sup>4</sup> An artifact in NCS is any recorded electrical potential that does not originate in the nervous system.<sup>5</sup>



**Figure 16-4.** Posterior tibial motor NCS performed with the E1 placed on the belly of the adductor hallucis longus (AHL), E2 placed 3 to 4 cm distal to E1 and the ground (G) placed in between the E1 and the stimulating electrodes. In this example, G has been placed on the lateral malleolus. The pictures illustrate the proper stimulation sites at the ankle and behind the knee. The stimulator polarity should be cathode (–) distal. The corresponding waveform provides an example of a normal CMAP elicited at that stimulation site.

Depending on the nature of the obstacle, corrections may range from simple to impossible. Regardless of the type of change that is necessary, the technologist must have enough knowledge to recognize the situation and handle it accordingly. In this section, we will discuss some common problems that arise in NCS.

### ELECTRICAL

Electrical refers to any source that is derived from an object outside of the body. These factors may be difficult to eliminate because they often occur from external devices over which the technologist has little or no control. Sixty-cycle interference is very common in inpatient units and during intraoperative monitoring. It is desirable to reduce the 60-Hz interference to an acceptable level. This can be achieved by addressing the contributing factors that the technologist can control.

### Machine Settings

Having the machine properly set up is very important for the accuracy of the results. Improper high and low filter settings

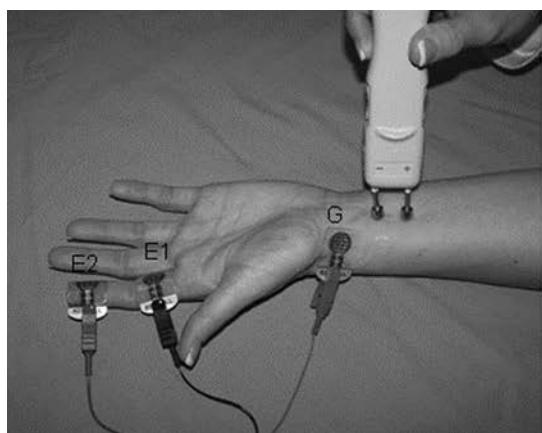
will alter the appearance of the response, providing the physician with inaccurate information. The technologist should also pay close attention to the sweep speed and sensitivity. Incorrect settings may lead to visual misinterpretation of responses caused by a narrowed visual field that masks vital information.

### Stimulus

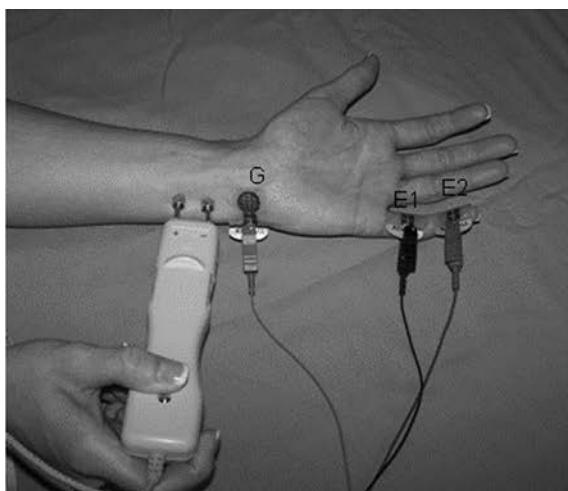
Stimulation artifact occurs when the machines' limits have been exceeded. Eliminating stimulus artifact may be impossible. This can become a nuisance, making it difficult to determine the proper onset of a response. This holds true especially for sensory nerve potentials, due to their sensitivity to external interference. The most successful way to eliminate stimulation artifact is to prep the skin, place the ground in between the stimulating and recording electrodes, keep an ample distance between the stimulator and E1, and not overstimulate the nerve being studied, which leads to volume conduction.

### Electrodes

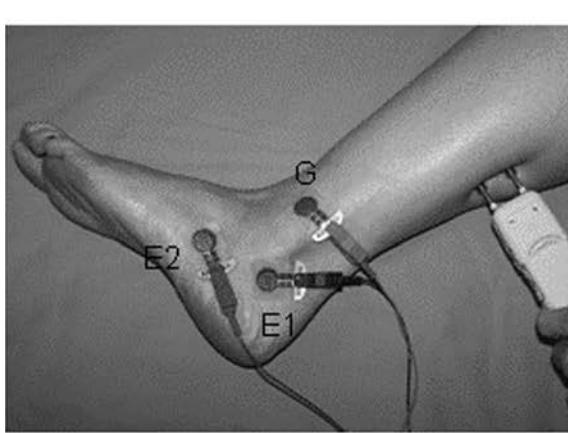
When choosing the appropriate electrodes to perform NCS, it is imperative that you select the proper size. If the electrode size



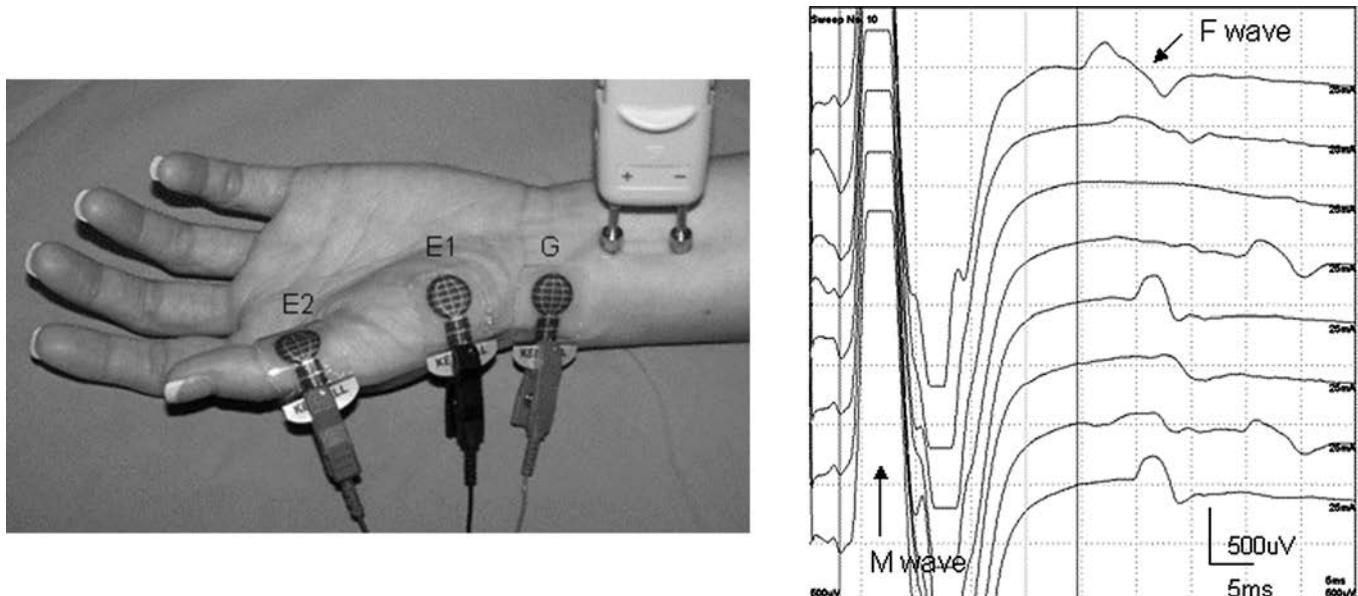
**Figure 16-5.** Median sensory NCS performed with the E1 placed on the index finger, E2 placed 3 to 4 cm distal to E1, and the ground (G) placed in between E1 and the stimulating electrodes. The picture illustrates the proper stimulation site at the wrist. The stimulator polarity should be cathode (-) distal. The corresponding waveform provides an example of a normal SNAP elicited at that stimulation site.



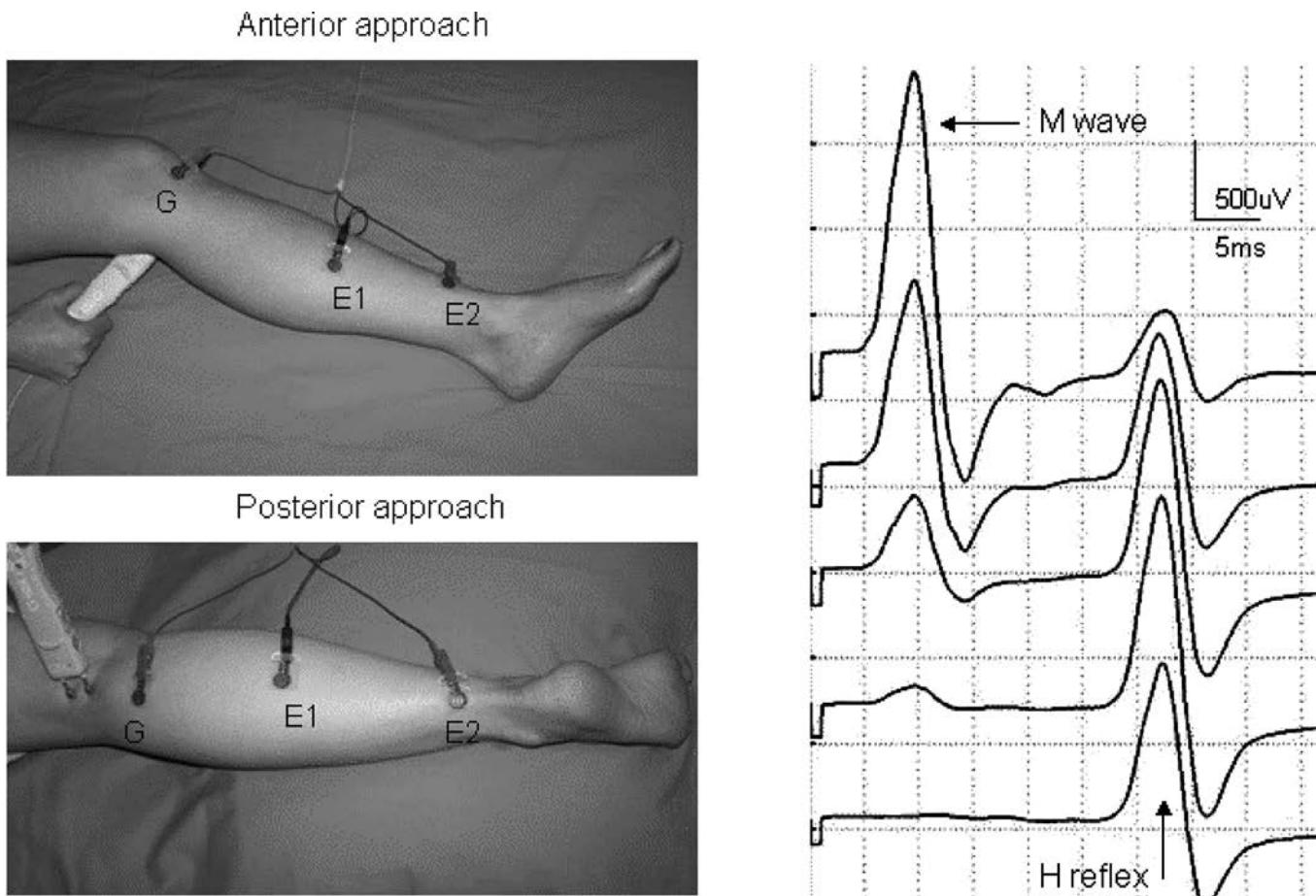
**Figure 16-6.** Ulnar sensory NCS performed with the E1 placed on the little finger, E2 placed 3 to 4 cm distal to E1, and the ground (G) placed in between E1 and the stimulating electrodes. The pictures illustrate the proper stimulation site at the wrist. The stimulator polarity should be cathode (-) distal. The corresponding waveform provides an example of a normal SNAP elicited at that stimulation site.



**Figure 16-7.** Sural sensory NCS performed with E1 placed posterior to the lateral malleolus, E2 placed 3 to 4 cm distal to E1, and the ground (G) placed in between E1 and the stimulating electrodes. The pictures illustrate the proper stimulation site 14 cm proximal to E1. The stimulator polarity should be cathode (-) distal. The corresponding waveform provides an example of a normal SNAP elicited at that stimulation site.



**Figure 16-8.** Median F wave study is performed using the median motor NCS setup (see Fig. 16-1). The picture illustrates the proper stimulation site at the wrist. The stimulator polarity should be cathode (–) proximal. The corresponding waveform provides an example of a normal series of F waves. This demonstrates the consistent M wave and the variable F waves.



**Figure 16-9.** **Anterior approach.** H reflex study is performed with the E1 placed half way between the knee and malleolus on the belly of the soleus, E2 is placed at least 4 cm distal to E1 on the tibia, and the ground (G) placed in between E1 and the stimulating electrodes. **Posterior approach.** H reflex study is performed with the E1 placed half way between the knee and malleolus on the belly of the soleus, E2 is placed at least 4 cm distal to E1 on the Achilles tendon and the ground (G) placed in between E1 and the stimulating electrodes. The pictures illustrate the proper stimulation site behind the knee. The stimulator polarity should be cathode (–) proximal. The corresponding waveform provides an example of a normal H reflex demonstrating the large M wave at a higher-intensity stimulation (**top**) and as the intensity is decreased the M wave amplitude decreases and the H reflex increases (**bottom**).

is too large, it cannot be properly placed over the individual muscle belly. This leads to a spread of anomalous fibers evoking an incorrect waveform, providing inaccurate amplitude and latency measurements.

## PHYSIOLOGICAL

Physiological artifacts refer to sources that are derived from the body. These factors vary among patients depending upon work habits, hygiene habits, physical stature, and ethnic origins. Most of these effects are unavoidable. However, as a technologist, one must follow standard procedures to minimize their appearance on the NCS screen.

### Skin Resistance

To ensure adequate results, every patient should have the skin prepped before the start of the study to reduce electrode impedance. Cleansing of soiled or sweaty skin can be achieved by wiping the areas to be tested with an alcohol swab. Calluses, oils, and other more stubborn types of resistance may require rougher skin prep. In these situations, a pumice scrub or a mild sand paper may be used to cleanse the area.

Reducing the amount of skin resistance is imperative. Having a good connection between the recording electrodes and the patient's skin (reduced impedance) plays a key role in acquiring clear, accurate wave forms.

### Temperature

The skin temperature of the patient being studied is a very important piece of information. A cold nerve cannot transmit the stimulation as quickly as a warm nerve, resulting in false-positive interpretations. If the skin temperature is below 32°C, the study may show slowed conduction velocities and increased latencies and amplitudes. Changes are more prominent in sensory studies, but are also noted in motor conductions. The best way to compensate for a cold limb is to warm the extremity to the desired temperature. However, warming is not always practical, so a mathematical equation applied to the measure-

ments corrects the results by about 4% per degree using 32°C as a normal temperature (Table 16.5).<sup>6</sup>

### Age and Height

The patient's age is significant because of the growth process of the nerves. Infants have slower latencies and conduction velocities due to the development rate of the myelin sheath that surrounds the nerve fibers. As a person ages, nerve responses tend to decrease in amplitude due to physiological axonal degeneration. The patient's height is important due to the fact that the electricity must travel further along the nerve to get from point A to point B. Without height adjustment, latency measurements and conduction velocities may appear abnormal if the patient's height is above average.

### Other Contributing Factors

Before beginning the NCS, the technologist should take a brief history. When doing so, there are four main questions that should be asked to determine the path of the study.

**MAIN COMPLAINTS.** The patient's main complaints should always be double checked to ensure the correct test is performed, that is, the correct side and limb is tested.

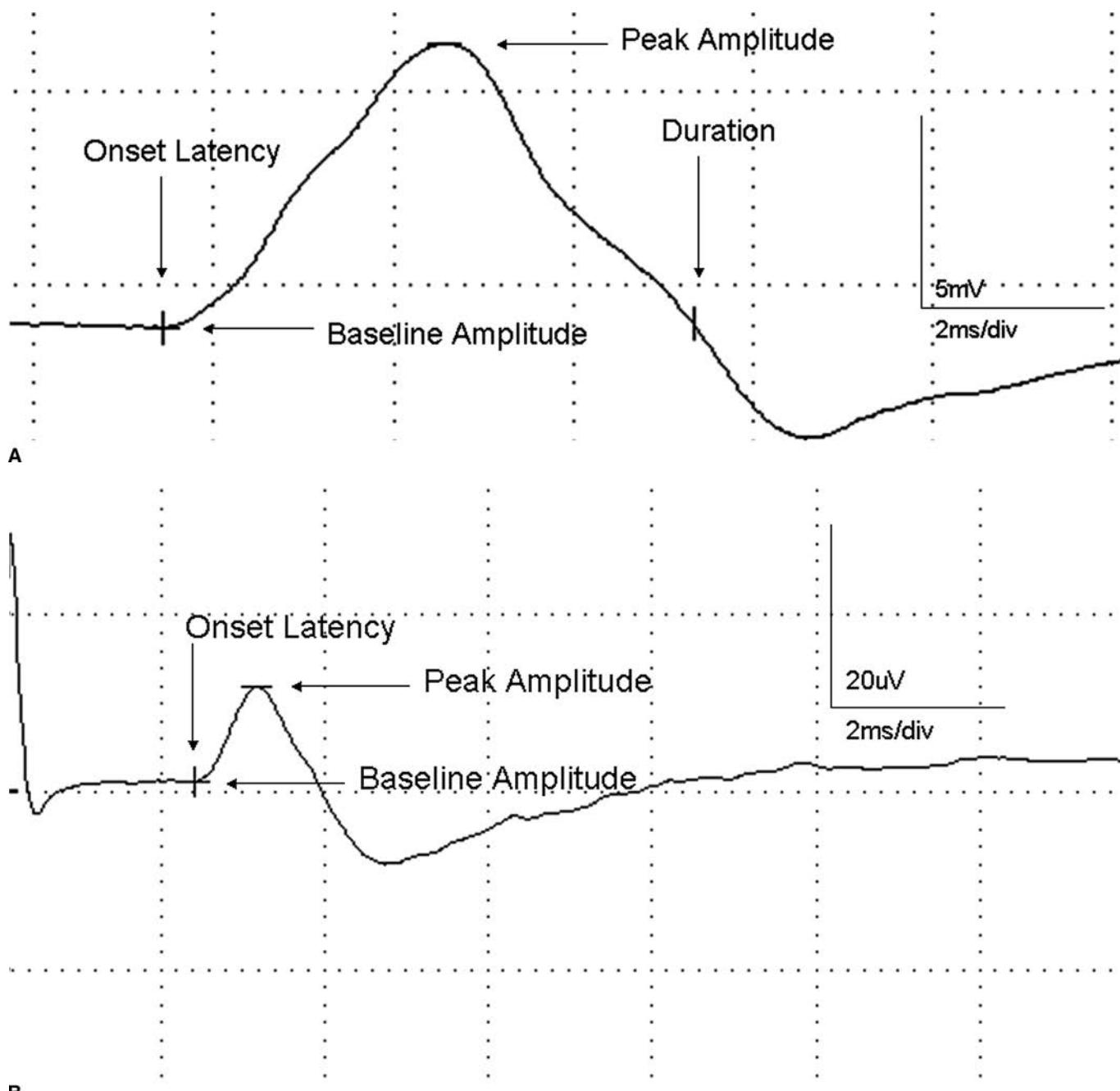
**MEDICATIONS.** Current medications should be noted, especially if the patient is taking a blood thinner (coumadin, heparin, or warfarin). Blood thinners do not affect the nerve conduction portion of the study. However, they do pose a risk of bleeding during the electromyography (EMG). Most physicians may choose to avoid or limit the EMG if the patient's international ratio (INR) level is above 2.0, which indicates an increased bleeding tendency. If repetitive nerve stimulation is required, it is also necessary to be aware if the patient is being treated for a neuromuscular junction disorder (such as myasthenia gravis) with Mestinon. Mestinon works by improving communication between the nerve and the muscle. A dose taken within 6 hours of testing can mask the results producing a false-negative study.

**TABLE 16.3** Example of a Motor and Sensory Conduction Velocity

<b>A. EXAMPLES OF A MOTOR CONDUCTION VELOCITY<sup>a</sup></b>				<i>Conduction Velocity (CV) (Wrist-Elbow)</i>
<i>Median Motor</i>	<i>Onset Latency</i>	<i>Latency Difference</i>	<i>Distance</i>	
Wrist	4.1 ms			
Elbow	7.5 ms	3.4 ms	210 mm	61.8 m/s
<b>B. EXAMPLE OF A SENSORY CONDUCTION VELOCITY<sup>b</sup></b>				
<i>Median Sensory</i>	<i>Onset Latency</i>	<i>Distance</i>	<i>Conduction Velocity (CV) (Digit-Wrist)</i>	
Wrist	3.1 ms	140 mm	45.2 m/s	

<sup>a</sup>Distance/Latency difference = CV or 210/3.4 = 61.8.

<sup>b</sup>Distance/Latency = CV or 140/3.1 = 45.2.



**Figure 16-10.** **A:** An example of the proper measurements used when marking a CMAP. **B:** An example of the proper measurements used when marking a SNAP.

**HISTORY OF DIABETES.** Diabetes is the number one cause of polyneuropathy. The technologist should be aware of a patient diagnosed with diabetes because it increases the chances of an abnormal study. Patients are commonly found to have an underlying diabetic polyneuropathy in addition to the areas of concern.

**PACEMAKERS AND DEFIBRILLATORS.** Pacemakers and defibrillators are not contraindicators for performing NCS.<sup>7</sup> However, the technologist should be aware if the patient has one installed and pay special care not to stimulate proximal segments that may trigger the device. These devices may also create an electrical artifact that can be visually recognized on the NCS screen.

**TABLE 16.4****Uncommon Motor and Sensory Nerve Electrode Placement**

Nerve	Active Electrode (E1)	Reference Electrode (E2)	Ground	Stimulation site
<b>A. UNCOMMON MOTOR NERVE</b>				
Radial	Extensor Indicis Proprius	3–4 cm distal to E1 on the head of the ulna bone	between the stimulating and recording electrodes	<i>Forearm:</i> Distal to the elbow beneath the brachioradialis <i>Above elbow:</i> Proximal to the spiral groove beneath the biceps brachii <i>Axilla:</i> <i>Erb's Point</i>
Long Thoracic	8th intercostal rib	3–4 cm below the E1	between the stimulating and recording electrodes	<i>Erb's Point</i>
Axillary	Deltoid	On the bony prominence of the shoulder	between the stimulating and recording electrodes	<i>Erb's Point</i>
Musculocutaneous	Biceps	On the bony prominence of the shoulder	between the stimulating and recording electrodes	<i>Erb's Point</i>
Spinal Accessory	Trapezius	On the bony prominence of the shoulder	between the stimulating and recording electrodes	Sternocleidomastoid
Phrenic	2 finger breadths below the xiphoid process	18 cm away from the E1, along the rib cage	between the stimulating and recording electrodes	Sternocleidomastoid
Femoral	Vastus Lateralis, 16–18 cm distal to the groin	Distal to E1, just above the knee	between the stimulating and recording electrodes	Groin- Lateral to the Femoral Pulse
Suprascapular	Infraspinatus and Supraspinatus	On the bony prominence of the shoulder	between the stimulating and recording electrodes	<i>Erb's Point</i>
<b>B. UNCOMMON SENSORY NERVE</b>				
Medial Antebrachial	8 cm distal to the elbow crease on the medial forearm	3–4 cm distal to E1	between the stimulating and recording electrodes	12 cm proximal to the active electrode
Lateral Antebrachial	12 cm to the elbow crease on the lateral forearm	3–4 cm distal to E1	between the stimulating and recording electrodes	In the lateral side of the elbow crease
Lateral Femoral Cutaneous	Vastus Lateralis, 16–18 cm distal to the groin	Distal to E1, just above the knee	between the stimulating and recording electrodes	Just above the inguinal ligament
Superficial Peroneal	Halfway between the lateral malleolus and tibialis anterior tendon	3–4 cm distal to E1	between the stimulating and recording electrodes	10 cm proximal to E1 on the lateral calf

**SUMMARY**

A good technologist should have the knowledge to independently provide information to the physician in order for them to properly evaluate nerve function.

NCS are helpful in determining the viability of the nerves. However, it is important to remember that NCS are only an

extension of the full neurological examination performed by the physician. The prior discussion should serve as an aid when performing NCS and should be considered as basic guidelines for all technologists.

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**TABLE 16.5****Formula for Temperature Conversion Equation**

$$\text{TCL} = \text{ML} - (0.04 \text{ ML})(32 - T)$$

Measured latency (ML) = 28.0

Step 1:  $28.0 \times 0.04 = 1.1$

Skin temperature (T) = 30°C

Step 2:  $32 - 30 = 2$

Temperature corrected latency

Step 3:  $1.1 \times 2 = 2.2$

(TCL) = 25.8

Step 4:  $28.0 - 2.2 = 25.8$

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