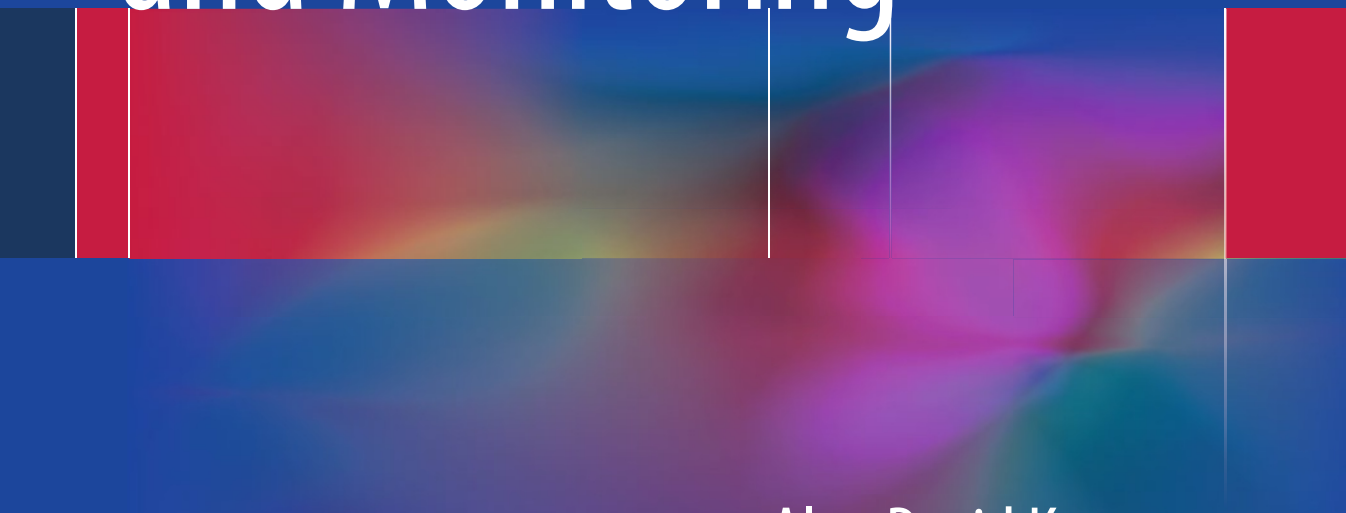
Principles of Neurophysiological Assessment, Mapping, and Monitoring



Alan David Kaye
Scott Francis Davis
Editors

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Foreword

In the constantly evolving realm of fundamental, translational, and clinical medical sciences, it is imperative that cutting-edge knowledge be synthetized and transmitted clearly and accurately to healthcare providers. This book deals with intraoperative monitoring, a field that has evolved rapidly in the last few decades. Intraoperative neurophysiologic monitoring has become an important area because it provides functional information in real time during surgery, thus benefiting patients and serving as an essential guideline for surgeons in the prevention of neurological damage. Therefore, multidisciplinary knowledge spanning neurophysiology, anesthesiology, neurology, and neurosurgery is enriching this field due to the creation of a two-way channel of communication, from the lab bench to the clinic and from the patient to the lab. This includes monitoring of the electrical activity of the nervous system (auditory and somatosensory evoked potentials and EEG).

That is where this book comes in: *Principles of Neurophysiological Assessment, Mapping, and Monitoring*. Based on their combined knowledge and experience in intraoperative neurophysiologic monitoring and neurophysiology in neurosurgery, Drs. Alan David Kaye and Scott Francis Davis have assembled a textbook that is a well-integrated blend of contemporary fundamental and clinical sciences aimed at clinicians who monitor the function of the nervous system during surgery. Dr. Kaye is an outstanding leader of the academic program in anesthesiology at the Louisiana State University Health Sciences Center (LSUHSC), New Orleans, and Dr. Davis has distinguished himself, due to his talent, drive, and motivation, since he was a graduate student in the LSUHSC Interdisciplinary Graduate Program.

While there are advanced texts leveled at neurophysiologists, surgeons, and residents alike, there are few that expound upon the basics of intraoperative neurophysiologic monitoring in such a way that those just entering the study can understand the underlying principles of this field. At the same time, the way that the materials are presented here also will be very useful to experienced specialists. The contributors to this book provide the brick and mortar that lay the foundations of neurophysiologic monitoring, which will benefit new technologists all the way to neurophysiologists and neurosurgeons.

Not unlike Wilder Penfield, who pioneered seminal brain mapping studies, this book seeks to provide a comprehensive guide to students just beginning their journey and experts searching for an excellent reference to other aspects of intraoperative neurophysiologic monitoring and neurophysiology in neurosurgery.

New Orleans, LA, USA Nicolas G. Bazan

Preface

Electrophysiological stimulation and recording was used in the operating room by researchers as early as the 1930s to study the functional organization of the cerebral cortex [1–4]. Seminal studies by scientists such as Penfield and Celesia led to our modern understanding of the functional organization of the cerebral cortex. This early work paved the way for further investigations into the utility of intraoperative electrophysiological recordings in protecting the nervous system during surgery. By the 1960s, facial nerve stimulation was being used during surgery for vestibular schwannoma to prevent postoperative facial nerve palsies [5, 6].

In the 1980s, brainstem auditory evoked potentials and somatosensory evoked potentials were introduced to protect the spinal cord and brainstem during surgery [7–9]. The application of intraoperative monitoring modalities began to cross into specialties other than neurosurgery such as orthopedics and ENT. This technology was still mostly available only at larger academic medical centers.

The 1990s ushered in a stage of rapid growth for the field of intraoperative monitoring. The advent of transcranial electrical stimulation provided a new means for monitoring the motor system during surgery [10]. Intraoperative monitoring began to move from the academic centers into community hospitals. This was made possible by the entry of private enterprise into the field, and with this growth came the demand for a skilled workforce. Traditionally dominated by physicians and neurophysiologists, the field now incorporated skilled technologists under the supervision of one of the physicians or PhD neurophysiologists.

Continued growth led to two new challenges in the delivery of IOM services to new markets: lack of formal training for IOM technologists and insufficient professional oversight. To a great extent, these problems are still present today. Someone interested in becoming an IOM technologist generally has to find a position with a company that has a quality training program. Corporate training programs range from the "see one, do one, teach one" model all the way to rigorous academic-quality programs. There are efforts to establish an academic path for people wanting to become IOM technologists. With job growth set to outpace qualified technologists, this problem will force a solution.

The problem of insufficient oversight was temporarily solved in the 1990s and early 2000s with the advent of real-time remote monitoring (RTM)

allowing the physician or neurophysiologist to monitor a case (or multiple cases simultaneously) and provide interpretation to the technologist and surgeon in real time. Once considered a luxury, RTM has become a community standard available nationwide. Currently only physicians are reimbursed for RTM, but a changing reimbursement climate and shortage of qualified physicians are posing a danger to patient access to RTM nationwide. In time it is likely that nonphysician providers, such as PhD neurophysiologists, will be reimbursed for providing RTM services.

Intraoperative monitoring is now entering a new and critical phase of growth. Emerging technology and advances in neuroscience research are creating exciting opportunities for the field of IOM. Neurophysiologists are working alongside neurosurgeons to map subcortical brain structures and identify therapeutic targets for treatment of movement and affective disorders. New minimally invasive surgical procedures are making recovery times shorter and reducing postoperative pain. These new procedures require different approaches to spinal cord and nerve root monitoring that will ultimately make spine surgery even safer. Finally, we are gaining more knowledge of basic neurophysiological function of patients under general anesthesia that will lead to new ways to monitor the nervous system. The study of spinal reflexes in the anesthetized patient is one promising example of the ongoing research that makes IOM an exciting and dynamic field.

The field of intraoperative monitoring requires foundational knowledge of several disciplines such as anatomy, physiology, surgery, electronics and instrumentation, and anesthesia. This book was conceived as a resource for a diverse audience. Primarily intended as a textbook for use in academic courses in intraoperative monitoring or in corporate training programs, this book is unique in that it provides a comprehensive section on anatomy and cellular neurophysiology relevant to the IOM clinician. This book is intended to be highly "reader friendly" and attempts to provide the didactic and practical principles needed for a new IOM clinician, experienced clinicians, anesthesiologists, and surgeons interested in intraoperative monitoring. Physicians, neurophysiologists, and technologists preparing for board exams will also find this text very useful. Basic didactic concepts presented in early chapters are brought together into practical chapters on intraoperative monitoring and mapping. Chapters covering electrophysiological assessment of spinal cord pathology and the treatment of pain round out this book and will be highly useful to anesthesiologists and residents interested in diagnosing and treating chronic pain.

New Orleans, LA, USA

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This book is dedicated to my incredibly talented wife, Robin, and our four perfect children (Georgia Rose, R. J., Scottie, and Graham). You are the light of my life and the source of all of my pride. Last, but not least, I dedicate my work *Ad maiorem Dei gloriam!*

New Orleans, LA, USA Scott Francis Davis

I would like to thank Scott Francis Davis for coming in my office and discussing his hopes to one day write the book presented here. I wish to thank my true love and wife, Kim, and my children, Aaron and Rachel. I want to thank my mother for stimulating and nurturing my interest in medicine, which began when she had lumbar disc surgery in 1975. Finally, I wish to thank my colleagues at LSU and Tulane Schools of Medicine for their support over the past 23 years.

New Orleans, LA, USA Alan David Kaye

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Introduction to the Operating Room

1

Kristin Krasowski Reed and Scott Francis Davis

Introduction

The IOM clinician is part of a patient care team that consists of the surgeon, nurses, technologists, and anesthesiologists. You will recognize that each team member has a specific role to fulfill in order to provide the best care for the patient. As an IOM clinician, you will spend the majority of your working hours inside a hospital operating room (OR). The OR is a unique environment that may take some time getting used to. You will encounter different types of equipment as well as rules for navigating the space and interacting with other team members. This chapter will introduce you to the operating room along with the equipment and personnel you will encounter there.

Going to the Hospital

Going to a new hospital can be a daunting task for even the seasoned neuromonitoring clinician. There are many hurdles that you must jump before you even meet the patient, from finding the appropriate place to park to navigating your way to the OR suite. Luckily, most hospitals have a similar layout.

Your journey begins with actually finding the hospital. You may often find yourself driving to a hospital in a new city in the early morning darkness. As you get closer, there are road signs that will help you to navigate the rest of the way in. These road signs are blue squares with a single white H (Fig. 1.1). Once you've found the hospital, you have to find an appropriate place to park. Dedicated patient or employee parking is often not permissible since the neuromonitoring service is considered a contracted vendor and not actual employees of the hospital. If you find dedicated visitor sections of the parking, that would be the best choice.

If this is your first trip to a new hospital, be familiar with the entry requirements for the facility you are visiting. For example, do you have to sign in at a security desk? Does the hospital use a third-party vendor credentialing service that has a self-service kiosk for you to obtain a badge? Maybe you need to visit the hospital biomed department to have your machine checked before bringing it to the OR. When in doubt, ask for assistance from hospital volunteers or security personnel. Once you have obtained a badge and had your machine checked (if required), you are on the lookout for the operating room. Begin by following signs to pre-op, post-op, or surgery.

The OR suite has multiple areas that you will learn to navigate, including the individual

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Fig. 1.1 An example of a road sign directing traffic toward the nearest hospital

operating rooms. Most operating suites have a similar layout (Fig. 1.2). Among the areas you will encounter are changing rooms (usually connected to a staff lounge), a control desk (also called the front desk or bridge), offices, a sub-sterile corridor connecting the individual operating rooms, and pre- and post-op holding areas. It is important to become familiar with which areas are restricted to personnel in scrub attire and which are not. These areas are often indicated with either a sign or a strip of red tape on the floor.

When first entering the OR suite, the first room you may come across is the locker room. Inside the locker room, scrub pants and tops will be available. You should arrive in professional clothing and change into hospital-provided scrubs upon entering the operating suite. Sometimes you will find empty lockers for visitor use. If you are concerned about the security of your valuables, you may wish to carry your own padlock. There is often an exit door into the OR corridor once you are dressed out in scrubs. Either inside or just outside the locker room will be bins with scrub hats and protective shoe covers. In the OR corridors, scrubs, hats, and shoe coverings are required; however, masks are not needed until entering the sub-sterile corridor or an OR that has open sterile equipment or a surgical procedure in progress.

Once dressed out, the first stop you should make is to the control desk to look at the board. The board may be either a traditional whiteboard or more sophisticated panel of LCD monitors. No matter if simple or sophisticated, the board contains all of the information on surgical procedures being performed in the operating suite that day. It will show information on the scheduled start time, room number, the procedure, and the surgeon. The board may indicate the current status of the procedure (in progress, delayed, etc.). You should always check the information on the board against the information you had prior to coming to the hospital. It is common to discover that the cervical fusion you thought you were monitoring is really a lumbar fusion or even that your case has cancelled or been delayed.

Now you are ready to go back to the room. If there is a sub-sterile corridor, you should enter the room from here. This is to limit the entry of air from the non-sterile corridors, which are generally only used to bring the patient into the room. If possible, get a cart and set your machine up in the sub-sterile area and bring it into the OR, leaving your machine case in the corridor. Remember your machine case has been sitting in your house and car as well as rolled through the parking lot. It might have dirt, pet dander, etc. on it. No one wants your cat's hair contaminating the room. If you are the first member of the OR team entering the OR, you do not necessarily have to have a mask on as nothing in the room is sterile yet. Once the equipment to be used during the surgery has been opened, all members of the team must have their masks on. This equipment is easily recognizable by the blue sterile packaging it comes in. Remember: in the OR blue equals sterile, which means that masks should be on and covering your face.

The individual operating rooms are well lit, slightly cooled, and humidity controlled to decrease the spread of infection. They have specialized air handlers that filter air and keep the pressure slightly raised. The positive pressure environment serves to push air out of the room when the door is opened in order to keep germs and insects out of the room.

Once inside the operating room, you will see many pieces of equipment. The room is set up strategically to maximize efficiency and minimize the

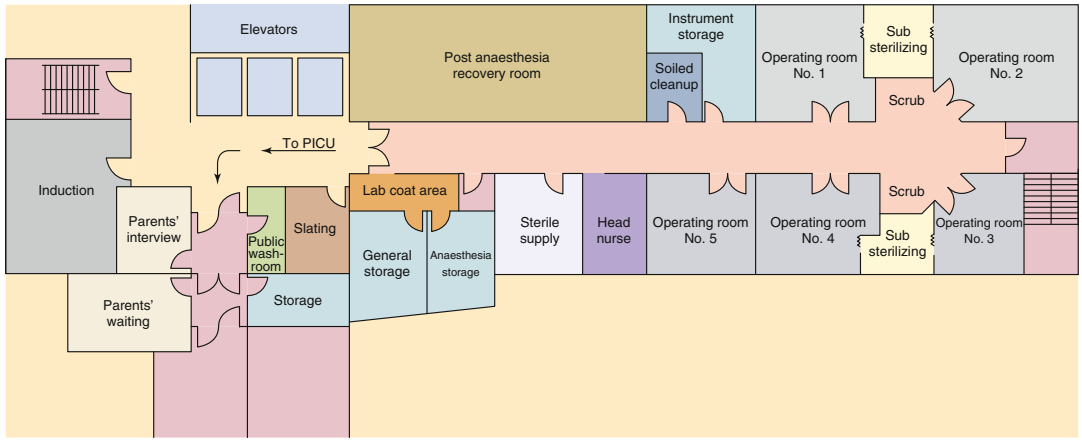

Fig. 1.2 Floor plan showing the layout of a typical operating suite

chance for infection. For example, the sterile table of instruments will be located on the opposite side of the room from the doorway. The operating table (sometimes called the bed) is usually in the middle of the room, and the anesthesia machine is located at the head of the operating table. Microscopes, neural navigation, and X-ray equipment (C-arms and O-arms) remain against the walls. They need to be brought in close to the bed. Remember that these larger items will be covered with a sterile drape before being used. It is permissible to touch these items before they are draped but not after.

When you first enter the OR, you should identify an appropriate place to set up and monitor the case. Always introduce yourself to the circulating nurse and politely ask where you should set up. Generally it is best to set up adjacent to the anesthesia machine. This location gives you good access to the patient as well as to the anesthesiologist or CRNA. By monitoring from this location, you avoid having to get up from your station to gather anesthesia information.

Pre- and Post-op Areas

Prior to being brought back to the operating room, the patient is held in a pre-op staging area. The period of time before the patient is brought to the room is a hectic one with all members of the team trying to gain access to the patient before the patient is anesthetized. It is during this time that consents for treatment (including monitoring) and past medical and surgical histories are obtained. The neuromonitoring clinician uses this opportunity to confirm the surgical procedure and levels as well as to identify any pre-existing pathologies that may affect the monitoring data. At the conclusion of the procedure, the patient is brought to the postoperative area, also called the recovery room. It is here that the monitoring clinician will assess the patient's postoperative neurological status.

The Surgical Team

Surgery should be considered a team sport. There is a unique cultural undercurrent that is present in the operating room that you will find no matter what part of the country you are working in. The surgeon is first and foremost the team captain. All members of the team must carry out their responsibilities with attention to the wishes of the surgeon. To help ensure consistency, each surgeon has preference cards that are reviewed by the surgical staff prior to the start of the procedure. Preference cards have information such as how the surgeon likes the patient positioned and prepped along with information on types of instruments that should be available.

If the surgeon is the team captain, the circulating nurse is the team manager. The role of the circulating nurse is to make sure the procedure runs safely and smoothly. The circulating nurse is in charge of how the room is to be set up (including on where the neuromonitoring team will do

their job), prepping the patient, and making sure that all of the equipment, instruments, and supplies are readily available during the procedure. The circulator also performs the time out prior to incision. The time out is a pause in activity allowing the team to confirm that the correct patient is in the room, the correct site of surgery has been marked, and if there are any known drug allergies. The circulating nurse is responsible for the medical care of the patient until the recovery room staff takes over.

The anesthesiologist is a physician responsible for putting the patient to sleep, maintaining the patient in an anesthetized state during the procedure, and waking the patient up after surgery. The anesthesiologist is responsible for the medical care of the anesthetized patient. An anesthesiologist may be responsible for multiple rooms simultaneously and must be assisted by a member of the anesthesia team that is always present with the patient. This may be an anesthesiology resident (an anesthesiologist in training) or a nurse anesthetist. A nurse anesthetist is known as a CRNA, which stands for certified registered nurse anesthetist. The neuromonitoring team must communicate effectively with the anesthesia team. The choice of anesthetic may greatly affect the success of neuromonitoring. It is important to remember that the priority lies with the anesthesiologist keeping the patient anesthetized and medically stable. With that in mind, it is paramount that the neuromonitoring team communicates clearly with the anesthesia team and shows deference to their critical responsibilities.

The surgical technologist or scrub tech is responsible for sterilizing the instruments and setting up the instrument table. During the procedure the scrub tech will hand the surgeon instruments and is responsible for counting supplies both before and after the procedure. This safeguard ensures nothing is left inside the operative site. The scrub tech may be a nurse but may be a graduate of a 2-year training program in surgical technology.

Intraoperative imaging techniques are often used during spine surgery to assist the surgeon with identifying the correct level and determining the adequacy of instrumentation. A radiology technologist is present in the room to operate the imaging equipment. The most commonly encountered imaging equipment in the OR is the C-arm. Since there may be multiple rooms requiring the services of the radiology tech, this person may come and go during the procedure.

If hardware or other implants are to be used during the surgery, there will be a representative (often called a "rep") in the room that is trained in the use of the hardware or implants. This person is a hybrid sales person/technician and is usually not authorized to lay hands on the patient. Instead this person guides the surgeon in the appropriate use of the product and is there to troubleshoot issues that arise with the use of the product.

Each member of the team has an important role to play in ensuring a safe and effective surgery. This team approach often results in a mutual respect among the members of the team. It is common to see all team members thanking each other at the conclusion of a surgical procedure (Fig. 1.3).

Commonly Encountered Equipment

The Operating Table

There are several different types of operating tables to meet the requirements for different surgical procedures. Most share some common features. The ability to adjust the height of the bed as well as its position is a critical feature. The OR table is one of the most common sources of 60 Hz noise seen in IOM recordings. The table may be unplugged when its controls are not being used in order to eliminate the source of noise (Fig. 1.4).

Electrosurgical Unit

The electrosurgical unit (ESU) is also called the electrocautery equipment. This equipment uses high-frequency current to cut through the skin and cauterize bleeding vessels. There are two common types of ESUs, a monopolar and a bipolar. Use of the ESU introduces a high-frequency artifact into the IOM recording that is difficult to average out. The IOM machine should be paused during cautery (Fig. 1.5).

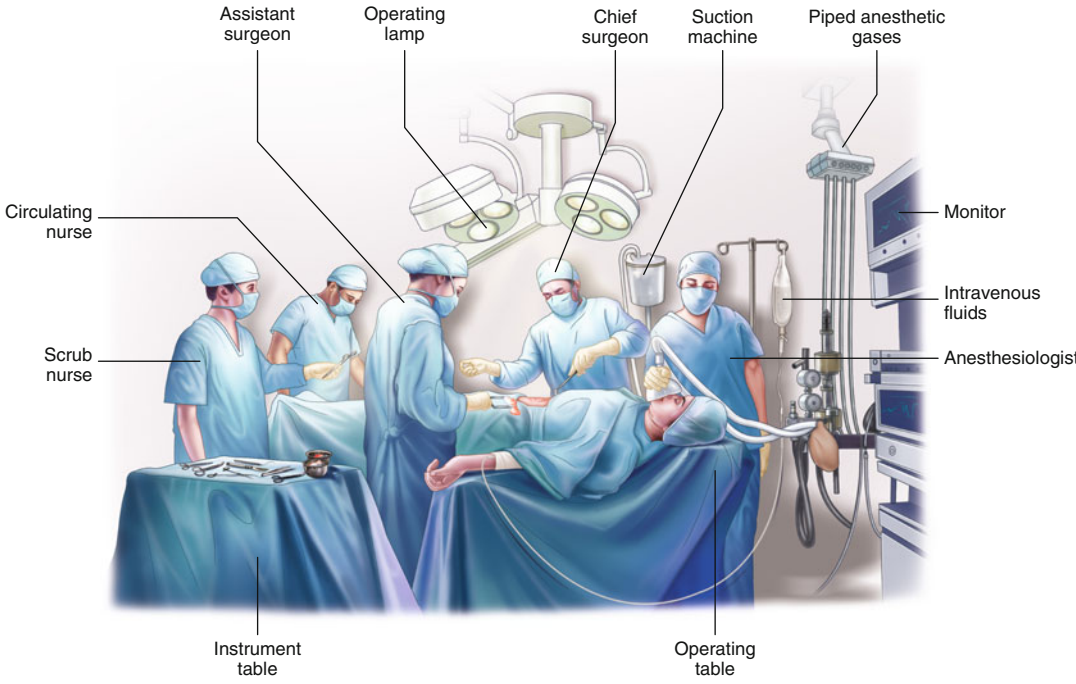

Fig. 1.3 Members of the OR team conducting a surgery

Fig. 1.4 A typical operating table

Fig. 1.5 The electrosurgical units are shown in the *top* and *middle* of the *blue cart*

Fig. 1.6 A C-arm. Notice the clear plastic drape used for sterility when the C-arm is being used. In this photo, the drape has been gathered around the top and is no longer sterile

C-Arm

The C-arm is an X-ray unit that can provide individual X-ray pictures or aid navigation using continuous fluoroscopy. The C-arm can rotate around the operating table for both anterior–posterior and lateral images and is used to guide the surgeon in the accurate placement of hardware (Fig. 1.6).

The Patient Warmer (Bair Hugger)

Patient warmers circulate warm air through a plastic blanket that is draped over the patient during surgery. These machines are often a significant source of electrical noise (60 Hz) introduced into the IOM recording.

The Microscope

The operating microscope is commonly used during intracranial and some spinal procedures. This type of microscope is large and often has two eyepieces allowing two surgeons to operate at once. The controls for the scope are located on the handgrips. There is the option of video output to a monitor allowing others in the operating room to have the same view as the surgeon (Fig. 1.7).

Anesthesia Work Area

The anesthesia work area is where you will find both the anesthesia machine and cart. The anesthesia machine is designed to deliver medical gasses and inhaled anesthetics to the patient during surgery. In addition there are several patient monitoring devices connected to display monitors. You will notice electrical outlets on the back of the anesthesia machine. These are for use by the anesthesia team only. IOM equipment should never be plugged into the back of the anesthesia machine so as to avoid a disruption in power to this critical piece of equipment (Fig. 1.8).

Fig. 1.7 A surgical microscope sterilely draped with a clear plastic drape

The anesthesia cart resembles a large tool chest (and sometimes a tool chest is actually used). The cart contains locking drawers for the storage of injectable medications (Fig. 1.9).

Aseptic and Sterile Environments

It is commonly believed that the operating room is a completely sterile environment. This isn't true. The definition of sterility is "free from infective organisms." It would be difficult to maintain the sterility of the entire room with all of the people that must enter and leave before, during, and after a case. Instead, the OR has both sterile and non-sterile components. The non-sterile components, however, are kept aseptic meaning as free of microorganisms as possible. Once an incision has been made, the patient becomes more vulnerable to infection. Therefore, all elements that are going to be in contact with the wound exposure are to be sterile. All other items are non-sterile, but aseptically cleaned.

Fig. 1.8 An IOM station set up behind the anesthesia machine

Fig. 1.9 The anesthesia work station shown at the head of the operating table

It is important to be aware of sterile and non-sterile areas of the operating room when moving about. Sterile areas are indicated by the presence of blue drapes that cover tables or Mayo stands where sterile equipment or instruments will be kept during the procedure (Fig. 1.10). Larger items that must remain sterile such as the microscope or C-arm (X-ray) will be covered with sterile clear plastic drapes. Sterilizing such large equipment itself isn't possible, so covering with a sterile drape achieves the same effect. When walking about the room, it is imperative that you keep a distance of at least 18″ from any sterile areas. It is advisable to keep sterile areas in front of you to avoid accidental contact from behind that you may not even be aware of. If any part of your body or clothing comes in contact with a sterile surface, don't panic, but do make the circulating nurse or another member of the surgical team aware of it so that they can redrape the area or re-sterilize the instruments.

Anything that will come in contact with the operative wound must be sterilized. The process of sterilization kills all microorganisms on the surface of the item and prevents the transmission of microorganisms from the item to the patient. Once the item is sterilized, personnel who are in sterile gowns and wearing sterile gloves are the only people that may handle it. Sterilization is achieved on-site by placing the items in an autoclave. The autoclave uses high temperature and pressure to kill all microorganisms on the items. Many disposables that are used in surgery are sterilized at off-site locations where they are manufactured. These items, often plastic, may undergo sterilization using a gas called ethylene oxide (EtO). This method of sterilization is used on any equipment that cannot tolerate the high heat of more traditional methods of sterilization. Sterile items are easily identified by being loosely wrapped in a blue cloth. Another indication that instruments are sterile is if they are laying in a metal tray on top of a table that is draped in blue. Prepackaged disposable items will usually be in double packaged in clear plastic with a label indicating that the contents are sterile.

In addition to sterilization of instruments that will come in contact with the operative wound, it is equally important to sterilize the area of skin where the incision is to occur. This is called skin prepping. Prepping a surgical site on a patient involves shaving the skin around the incision,

Fig. 1.10 A surgical technologist stands in the foreground opening sterile items and placing them on the sterilely draped tables as indicated by the *blue drapes*. In the background, an anesthesiologist gets ready for the patient

scrubbing the skin with a disinfectant solution such as iodine, and then outlining this newly sterile area by taping a blue sterile drape to the patient's skin. This process creates a sterile window in which the surgeon will work. All personnel that will have contact with the instruments or the operative wound must be "scrubbed in." This means that they must carefully scrub their hands, fingernails, and arms and then don a sterile gown over their scrubs as well as sterile gloves. Personnel that are scrubbed in are to be considered sterile from fingertips to elbows and waist to shoulders (Fig. 1.11). They are not considered sterile from the waist down or from behind. Once someone is scrubbed in, you should avoid contact with these areas of their body, and they will avoid contact with any surface that is non-sterile. The members of the surgical team that go through this process are the surgeon, the surgical technologist (often called the scrub tech), and any other personnel assisting the surgeon with the procedure such as a physician assistant.

It is the responsibility of all team members to help avoid the spread of infection. Hand washing is the number one defense against infection both in and out of the OR. Hands should be washed before and after contact with each patient, when

Fig. 1.11 An example of personnel "scrubbed in." Notice they are sterile in the front from the waist up and from the fingertips to the elbows

hands are visibly soiled, and when there has been any contact with surfaces suspected of containing microorganisms. The proper technique for washing hands includes wetting the hands and applying soap and then scrubbing the hands thoroughly up to the forearms for a minimum of 20 s. Hands should then be rinsed in warm water and dried with a clean towel. Hand washing for the processes of "scrubbing in" is a more methodical process that involves a long-acting antimicrobial soap, scrubbing each fingernail in detail, and always scrubbing up to the elbows. This procedure takes a minimum of 5 min.

Communication and Documentation

A team is only as good as the weakest member. Each member of the team should understand their role and seek to carry that role out to the best of their ability, leaving behind any distractions or personal issues. The goal of each team member is to ensure a safe and effective surgical procedure. Achieving this goal requires proper communication and documentation. In order for the surgeon to concentrate on the procedure at hand, he or she must trust that the patient is being properly cared for and monitored by other members of the care team.

The neuromonitoring clinician must work with both the anesthesiologist and the surgeon to successfully accomplish the mission of monitoring the patient's nervous system during surgery. Information relayed from the neuromonitoring team to the surgeon or anesthesiologist can change the course of the surgery and avoid a negative neurological outcome for the patient. Inaccurate information regarding neuromonitoring data can harm the patient either by failing to detect an emerging injury or by creating a necessary pause or stop to surgery based on a false alarm. To ensure a successful outcome, three-way communication between the surgeon, anesthesiologist, and neuromonitoring clinician is essential.

It is essential that the communication between the surgeon, anesthesiologist, and neuromonitoring clinician be well documented. The IOM clinician should have conversations with the surgeon and anesthesiologist regarding the monitoring plan prior to the patient coming back to the OR. As the neurophysiological monitoring expert, you should present an appropriate monitoring plan to the surgeon for approval. The surgeon will have the opportunity to ask questions about a particular modality or to request that changes are made to the monitoring plan. It is much more difficult to have this conversation in the OR during the busy process of preparing for surgery. This conversation should be documented in the monitoring record, especially if the surgeon's requests are outside of commonly accepted monitoring protocols. Communication with the anesthesiologist prior to surgery is also essential. You should discuss the monitoring plan with the anesthesiologist including the effects of particular anesthetic regimens on the ability to collect monitoring data. At this time, contraindications to motor evoked potentials should be discussed as well as the location of all needle electrodes. If running motor evoked potentials, ask that the anesthesiologist place a soft bite block bilaterally. Document these communications thoroughly in the monitoring record.

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Anatomy of Intraoperative Monitoring

2

Scott Francis Davis

Introduction

Structure and function are intimately related. There is an old adage that structure subserves function. This is at once a simple and yet profound statement. Look around your environment and you will prove this concept to yourself time and again. A coffee cup, by necessity, has a hole at the top and not at the bottom. Its structure subserves the function of holding coffee. The human body is no less practically created. As an IOM professional you are tasked with protecting neural structures and functions at risk during surgery. An intraoperative neurophysiologic monitoring curriculum therefore must include a foundation in anatomy.

The neuromonitoring professional doesn't require a detailed knowledge of all anatomical systems but instead benefits from a more focused approach to relevant organs and systems that are directly involved in the monitoring plan. Generally, knowledge of the nervous, skeletal, and muscular systems is the cornerstone of the monitorist's anatomy curriculum. Equally important is the ability of the monitorist to communicate with other members of the care team using accurate anatomical terminology. This chapter provides an easily readable general overview of anatomical terminology and structures important to the neuromonitoring clinician with no previous background in anatomy.

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Directional Terminology

The location of anatomic structures can be described using directional terms recognizable by all healthcare professionals. The use of proper directional terminology is necessary to avoid ambiguity with regard to anatomic locations and patient positioning. The most important thing to remember is that the position of anatomical structures can only be described relative to another structure or landmark. For example, the question "Is the thumb medial or lateral?" must prompt the follow-up question "medial or lateral to what?" A correct question would be "Is the thumb medial or lateral to the pinkie?" When answering questions such as this, it is always necessary to place the patient in proper **anatomic position**. Anatomic position is defined as the patient standing erect with the feet facing forward and slightly apart (Fig. 2.1). The hands are down at the sides with the palms facing forward. If we go back to our sample question, we say that the thumb is lateral (further from midline) to the pinkie. If we rotate the patient's hand such that the palms are now facing behind, the answer to our question did not change! This is because we must always reorient the patient to the anatomic position in our mind.

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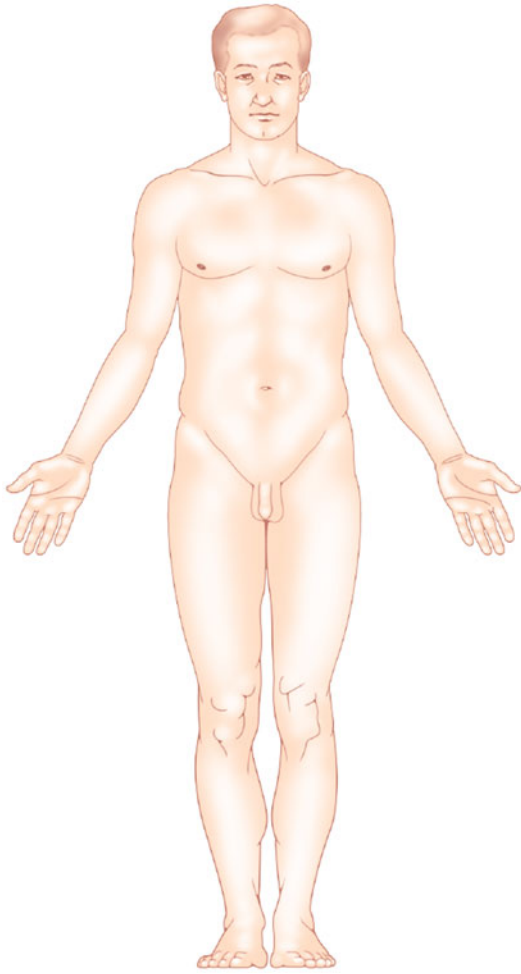

Fig. 2.1 The human body in anatomic position

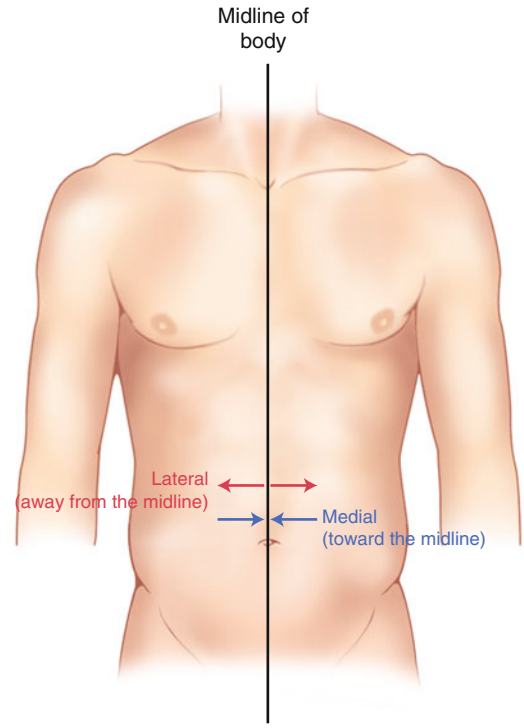

Fig. 2.2 Drawing of a human torso with the anatomic midline shown in *black*. *Arrows* indicate the relative terms of medial and lateral

The human body has a line of symmetry that bisects the body into right and left equal halves. This line of symmetry is known as the **midline**. Structures relatively further from midline than a reference structure are **lateral**, while structures lying closer to midline are said to be **medial** to the reference structure (Fig. 2.2).

The terms **proximal** and **distal** refer to locations that are closer to or further away from the point of attachment of a limb. These terms are often used to describe the position of structures along a limb relative to each other. For example, the elbow is distal to the shoulder but proximal to the wrist.

Superior and **inferior** are terms that refer to the position of a structure either above or below a reference point, respectively. For example, one can expect to find the nose superior to the chin in most people.

Humans, being bipedal, require some additional terminology than our quadruped friends. In other organisms, the terms anterior and posterior have different meanings than dorsal and ventral. In humans we often speak of the **anterior** and **posterior** portions of a limb or the torso. The anterior side is "belly side," and the posterior is "back side." These terms are synonymous with **ventral** and **dorsal**, respectively (Fig. 2.3). We begin to confuse these terms when considering directionality along the neuraxis.

The curvature of the neuraxis necessitates the introduction of two additional directional terms: **rostral** and **caudal**. The term rostral (from the Latin for nose) refers to points located further toward the nose on the neuraxis than the referenced structure. Caudal (from the Latin for tail) refers to points located further toward the end of the spinal cord. The rostral–caudal axis will bend

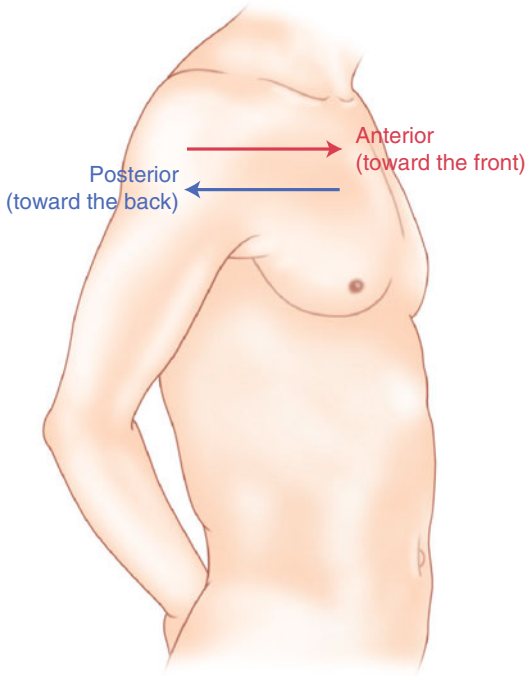

Fig. 2.3 A lateral drawing of the human trunk with *arrows* indicating the relative terms of anterior and posterior

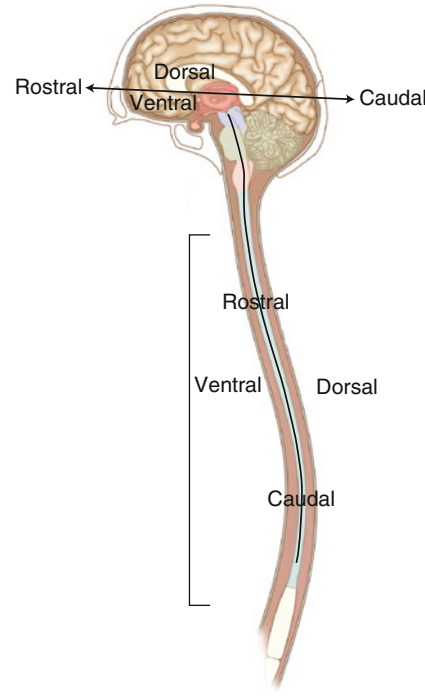

Fig. 2.4 A drawing of the neuraxis illustrating the relative terms rostral, caudal, dorsal, and ventral

with the neuraxis (most notably as you approach the level of the cerebral cortex). The dorsal–ventral or anterior–posterior plane is perpendicular to the rostral–caudal axis at any given point (Fig. 2.4).

Pathways moving from the peripheral nervous system toward the central nervous system are termed afferent pathways. These pathways are sensory. Pathways that travel from the central nervous system out toward the periphery are termed efferent pathways. These pathways carry motor information.

Organization of the Nervous System

The nervous system can be divided both anatomically and functionally. Anatomically we divide the nervous system into the central and peripheral nervous system. The central nervous system (CNS) consists of the brain, spinal cord, and the retina. The peripheral nervous system (PNS) consists of all of the nerves that come off of the brain (cranial nerves) and spinal cord (spinal nerves), nerve plexuses, and peripheral nerves innervating the various structures of the body.

Functional divisions of the nervous system include the somatic and autonomic divisions. The somatic nervous system governs voluntary actions and provides motor output through the action of the skeletal muscles. We will spend the majority of time discussing the somatic nervous system, as it is the division that is amenable to neuromonitoring. However, a brief consideration of the autonomic nervous system is warranted.

Autonomic Nervous System

The autonomic nervous system governs "automatic" visceral or vegetative functions and operates generally at the unconscious level. Examples of functions under autonomic control include respiration, heart rate, digestion, and sexual arousal.

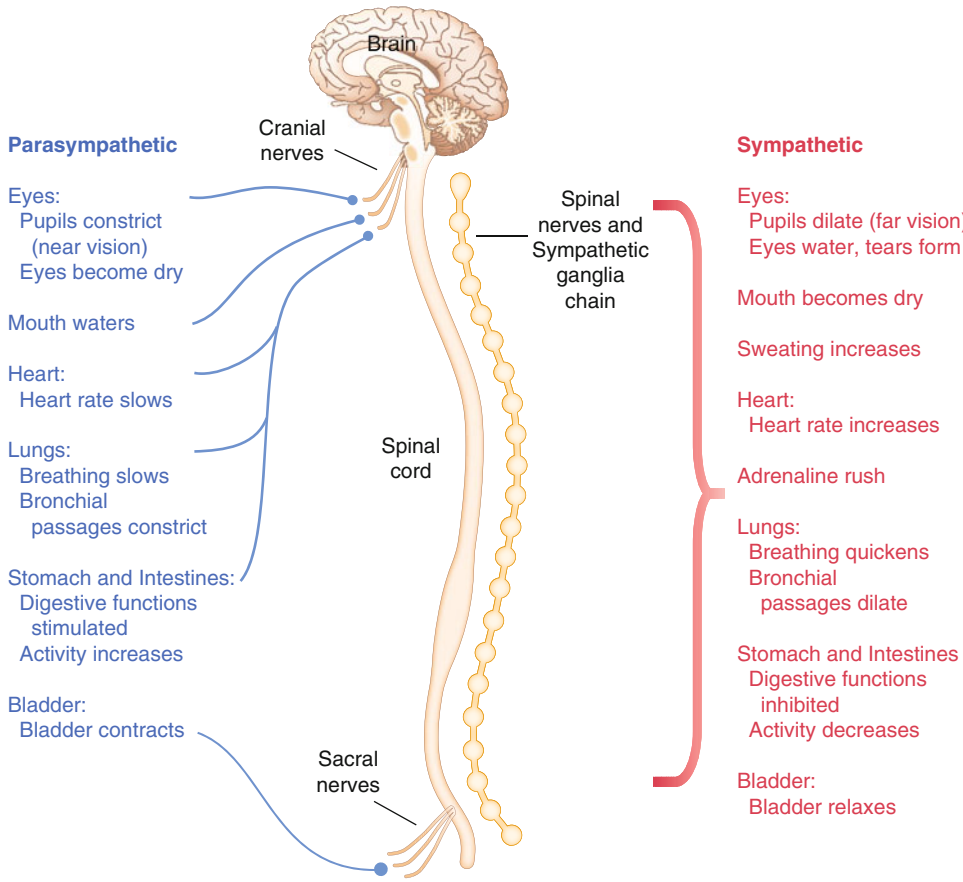

Fig. 2.5 The organization and function of the autonomic nervous system are shown. The parasympathetics are shown in *blue* on the *left* originating from cranial nerve nuclei and sacral spinal nerves. On the *right*, shown in *red*, are the sympathetics originating from thoracolumbar spinal nerves

The autonomic nervous system has two divisions: sympathetic and parasympathetic (Fig. 2.5).

The sympathetic nervous system has its anatomic origin from the thoracolumbar segments of the spinal cord, which is why it is sometimes called the thoracolumbar division of the autonomic nervous system. The sympathetics are responsible for the well-known "fight or flight" response. Consider what would happen if you were to encounter a bear in the woods (or any foreboding situation that you can imagine). Your body would prepare to either fight the bear or run from it. To do this you would need increased oxygen delivery to your muscles. The result is an increase in respiration and heart rate. Your pupils would dilate in order to increase visual acuity, and your hair would stand on end so that you may appear more ferocious to the bear (this last part may be an evolutionary leftover).

The parasympathetic division is anatomically located on either side of the sympathetic division and is alternately called the cranial–sacral division. The prefix "para" meaning "alongside" will remind you of the location. The parasympathetic division of the autonomic nervous system regulates visceral functions at rest. The phrase "rest and digest" summarizes the function of the parasympathetic system. You will study the cranial nerves in another section, but if a cranial nerve has an autonomic function, you can be sure it's parasympathetic. Again, remember that the parasympathetics have cranial or sacral origins. The vagus nerve (CNX), for example, is the largest parasympathetic nerve in the body.

Somatic Nervous System

The somatic nervous system governs voluntary movement as well as sensory processing of sensory information from external stimuli (such as light, sound, and touch). The somatic nervous system is that division that is tested during intraoperative monitoring. The somatic nervous system works through the activation of skeletal muscles and exteroceptors.

When discussing the somatic nervous system, it is common to specify between sensory and motor pathways. Sensory pathways are those that are activated by sensory stimuli in the environment and transmit this information to the central nervous system. There are many different sensory stimuli in our environment from light and sound to pain and temperature and many modalities in between. In order to be interpreted by the nervous system, these sensory modalities must be changed into electrical impulses. The process by which sensory stimuli are converted to electrical impulses for use by the nervous system is called **transduction**.

All sensory neurons have specialized endings called **exteroceptors** that are specific for the sensory modality they mediate. For example, exteroceptors in the retina are called photoreceptors. Hair cells are the sensory cells of the auditory system. Sensory neurons that mediate various types of mechanical stimuli in the skin have different names like Pacinian corpuscles for deep touch and pressure or Meissner's corpuscles for light touch (Fig. 2.6). Proprioception, knowing where your limbs are in space, is mediated by stretch receptors located in the muscles.

We are able to stimulate and record from both sensory and motor pathways in order to assess their function either in the clinic or during surgery. We will continue our discussion of neuroanatomy with a focus on sensory and motor tracks of the somatic nervous system. In subsequent

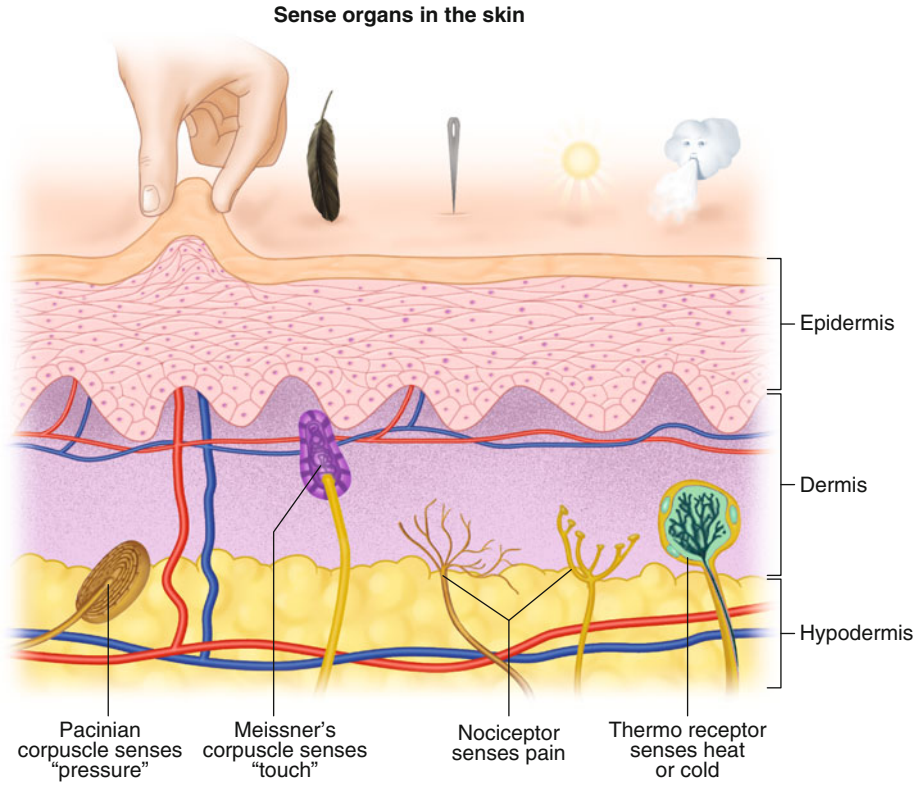

Fig. 2.6 Various sensory organs of the skin along with their function

chapters you will learn how we can stimulate and record from these anatomical substrates for the purposes of intraoperative monitoring.

Brain Anatomy

The human brain is arguably the most complex structure in existence. The brain governs all of human behavior. Vegetative functions are controlled by the lower brain structures of the brainstem, while reasoning and other distinctly human behaviors are a result of processing in higher brain centers such as the cerebral cortex. An understanding of the overall structural organization of the brain with a focus on sensorimotor processing is required for the IOM clinician to properly plan, carry out, and interpret a monitoring session. In this section we will discuss the gross anatomical organization of the brain including topographical organization. We will consider some important neural pathways in a subsequent section.

The Skull

The brain is protected by a bony structure called the **cranium**. The cranium, along with the mandible, makes up the **skull** (Fig. 2.7). The uppermost part of the skull is known as the skull cap or **calvarium**. The skull serves as a protective case for the brain. Bones of the skull are joined together by special immobile joints known as **sutures**. In infants, the skull bones are separated by cartilaginous areas known as **fontanelles** (Fig. 2.8). The fontanelles allow for expansion of the skull to accommodate the growth of the brain. The fontanelles are mostly ossified by 2 years of age.

The Meninges

The brain and spinal cord are further protected by a system of membranes called **meninges**. The meninges consist of three layers that are anatomically continuous: the **dura mater**, the **arachnoid**

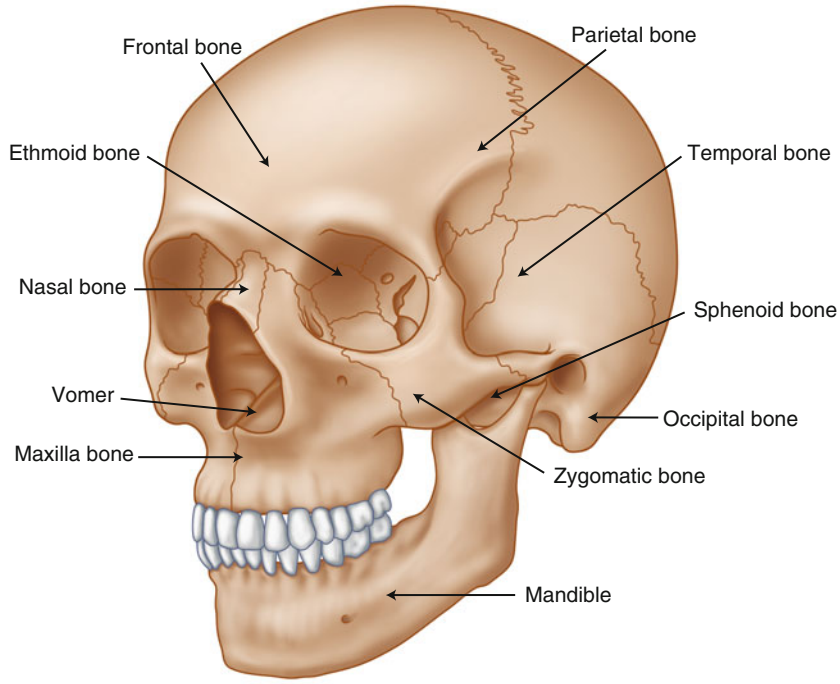

Fig. 2.7 The cranial bones including the frontal, parietal, temporal, and occipital bones along with the mandible comprise the complete human skull

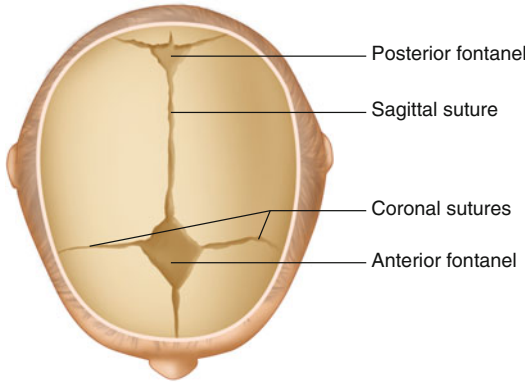

Fig. 2.8 Superior view of the infant skull showing the anterior and posterior fontanelles along with the development of the sagittal and coronal sutures

mater, and the **pia mater**. The term dura mater is from the Latin literally meaning "tough mother," while pia mater means "soft mother." The word arachnoid implies a spider weblike quality. The function of the meninges is to protect the brain and contain cerebrospinal fluid (Fig. 2.9).

The dura mater is the fibrous outermost layer of the meningeal membranes. This layer contains larger blood vessels as well as sensory nerve fibers. Among the blood vessels present in the dura mater are large venous sinuses that return blood and cerebrospinal fluid from the brain back to the heart. There are two dural extensions that you should be familiar with. The **falx cerebri** separates the cerebral hemispheres and the **tentorium cerebelli** separates the occipital lobe from the cerebellum (Fig. 2.10).

The arachnoid mater is thinner than the dura and resembles a loose fitting sac for the brain. Thin filaments known as **arachnoid trabeculae** extend from the arachnoid to the pia mater.

The pia mater is the thinnest layer of the meninges and closely adheres to the surface of the brain and spinal cord following each gyrus and sulcus. The pia has an extensive capillary network that nourishes the surface of the brain and spinal cord.

There is a normally occurring space between the arachnoid and pia mater. This **subarachnoid space** is filled with cerebrospinal fluid. Bleeding into this space as a result of trauma or the spontaneous rupture of a blood vessel can enlarge this space causing compression on the brain. This is known as a **subarachnoid hemorrhage** and requires surgical intervention to decompress the neural tissue. The dura and arachnoid are normally attached closely. Occasionally bleeding resulting from trauma or disease will occur opening up a space between the dura and arachnoid that does not normally exist. This potential space is called the **subdural space**, and the resulting bleed or clot would be known as a **subdural hemorrhage** or **subdural hematoma**, respectively.

The Ventricles

There are a series of canals within the brain whose function is to circulate cerebrospinal fluid. These are known as the **cerebral ventricles** (Fig. 2.11). There are two paired (left and right) lateral ventricles, a third ventricle, and a fourth ventricle. The ventricles communicate with each other via foraminal openings and are continuous with the central canal of the spinal cord. The left and right ventricles communicate with the third ventricle through the intraventricular foramina (of Monro). The third ventricle communicates with the fourth through the cerebral aqueduct (also known as the aqueduct of Sylvius). Cerebrospinal fluid returns to the subarachnoid space and venous circulation from the fourth ventricle via the midline foramen of Magendie and two paired foramina of Luschka.

The **cerebrospinal fluid** (CSF) bathes and cushions the brain and spinal cord and is contained within the dura mater. The CSF is produced by tufts of tiny capillaries called **choroid plexus** that are found within the ventricles (Fig. 2.12). CSF is simply filtrated blood plasma. CSF comes from the blood and must eventually return to the blood. The presence of microorganisms or white blood cells in CSF indicates infection within the central nervous system. CSF can be sampled for diagnostic purposes by lumbar puncture.

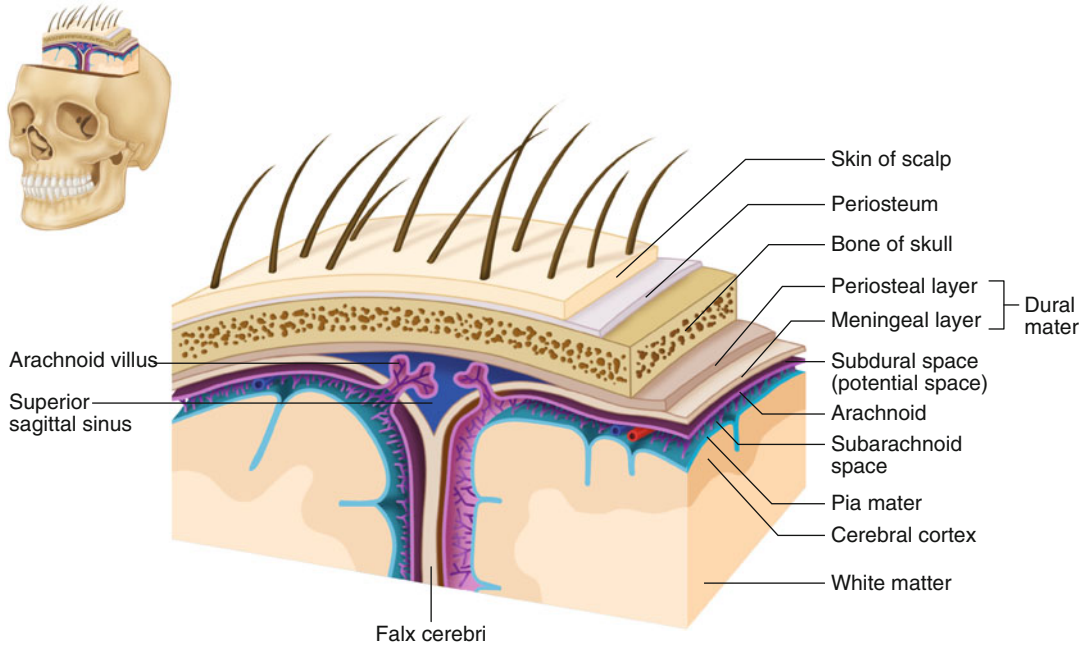

Fig. 2.9 The organization of the meninges and meningeal spaces of the brain

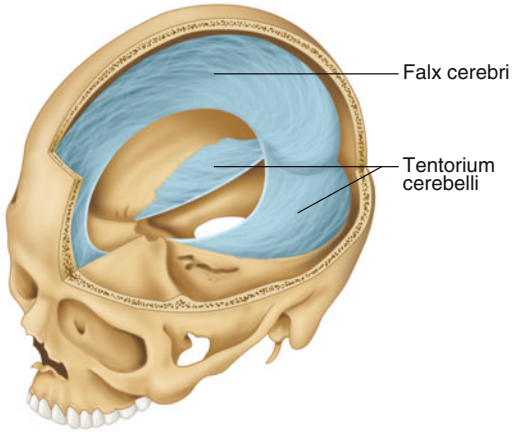

Fig. 2.10 The specialized dural infoldings: falx cerebri and tentorium cerebelli

The Cerebral Lobes

The cerebral cortex can be divided into four paired functional lobes: frontal, parietal, temporal, and occipital (Fig. 2.13). The cortex is the substrate for all higher order sensorimotor processing and cognitive functioning. If you recall the adage "structure subserves function," it won't be a surprise that the wrinkled structure of the cerebral cortex serves to increase surface area without necessitating an obnoxiously large skull to house the brain! Think of this as folding a piece of paper up to fit into your pocket. The bumps along the brain are called gyri (the singular form is gyrus), and the grooves separating the gyri are known as sulci (the singular form is sulcus). Each gyrus and sulcus of the brain has its own name. We will just consider a few.

The frontal lobe is responsible for higher order executive functioning such as personality, inhibition, and long-term memory. From the perspective of the intraoperative monitoring clinician, the frontal lobe is important because it governs voluntary motor function. Premotor and supplementary motor areas of the frontal lobe are not completely understood but are generally accepted to participate in planning of movement and coordination of sensory and motor information. Direct voluntary motor control, however, begins on one particular gyrus of the frontal lobe known as the **precentral gyrus**. The precentral gyrus

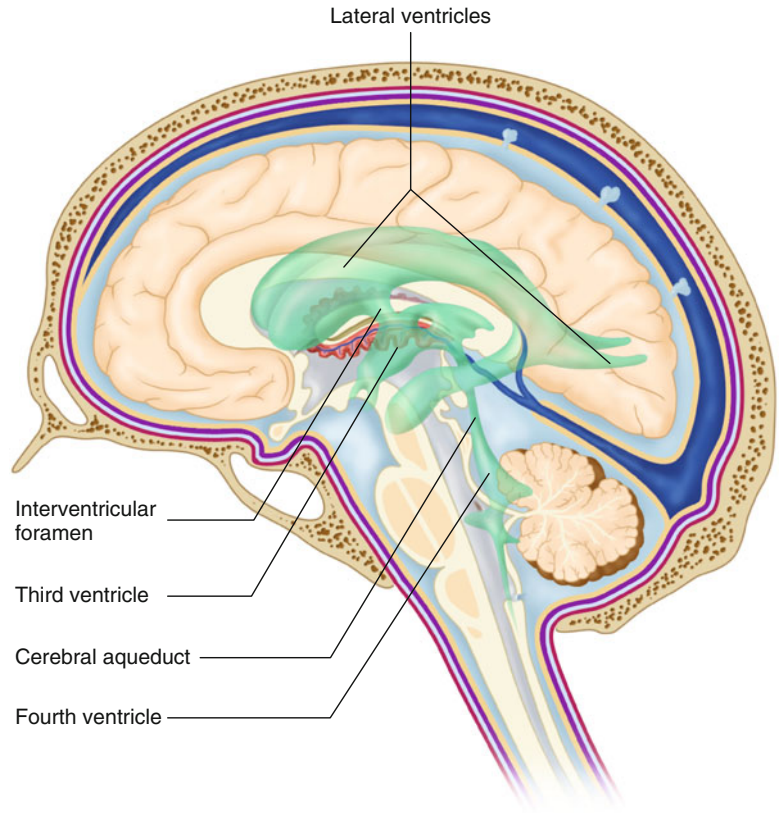

Fig. 2.11 The organization of the cerebral ventricles

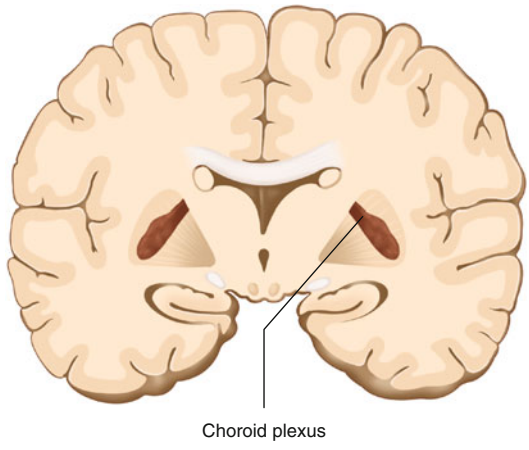

Fig. 2.12 The choroid plexus lines the ventricles making CSF

gets its name from its location anterior to the **central sulcus**. The central sulcus separates the frontal from the parietal lobes of the cerebral cortex. The precentral gyrus is also known as the **primary motor cortex**. Neurons of the precentral gyrus project directly to the spinal cord to influence voluntary movement.

Logic tells us that if there is a precentral gyrus then there must be a **postcentral gyrus**. This gyrus is located in the parietal lobe just posterior to the central sulcus and is also known as the **primary sensory cortex**. Neurons in the postcentral gyrus receive input from the somatic sensory pathways (Fig. 2.14).

The lateral sulcus (also known as the Sylvian fissure) separates the frontal and parietal lobes from the temporal lobe. The temporal lobes are responsible for the formation of short-term memories as well as speech and language comprehension.

The occipital lobes are the most posterior lobes of the cerebral cortex. The occipital lobes are the site of visual processing. The calcarine

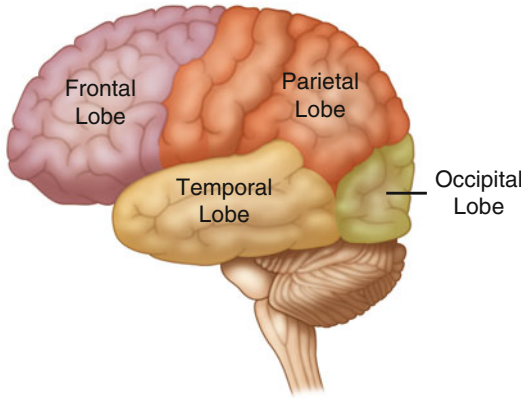

Fig. 2.13 The anatomic lobes of the cerebral cortex

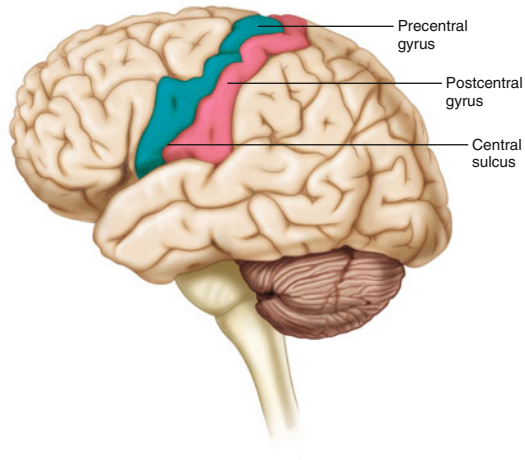

Fig. 2.14 The central sulcus shown with the precentral gyrus (primary motor cortex) and postcentral gyrus (primary sensory cortex)

sulcus separates the parietal and occipital lobes. This sulcus runs deep and is not completely visible from the cortical surface.

Topographical Organization

A common theme running through the nervous system is topographical organization. One of the main examples of topographical organization within the brain is the homunculus. The primary motor and primary sensory cortex are functionally organized such that a visual representation of the body may be reconstructed on them (Fig. 2.15). There are slight differences between the motor homunculus and sensory homunculus, but overall they are quite similar. You will notice that the hands and feet of the homunculus are quite large. This is because there is a proportionately large amount of surface area dedicated to these structures on the cerebral cortex. The hand and face areas are represented laterally, while the lower extremities and genitalia are represented medially. Correlating homuncular topography with cerebral blood supply and recorded electrical potentials will be important for intraoperative monitoring. You will soon learn that the middle cerebral artery supplies the lateral portions of the cerebral hemispheres and the anterior cerebral artery supplies the medial portion of the hemispheres. Deficits resulting from an MCA territory infarct will present clinically in the upper extremity and face. Deficits resulting from an ACA infarct will present clinically in the lower extremity. The homunculus has practical use when determining sites to stimulate and record from the brain for intraoperative monitoring.

The Diencephalon

The diencephalon is a region of the neuraxis, rostral to the midbrain, composed of a group of deep brain structures including the thalamus and hypothalamus (Fig. 2.16). The hypothalamus is often called the master endocrine gland of the body. The thalamus is a bilateral structure composed of several functionally distinct nuclei (Fig. 2.17). Sensory information on its way to the cortex is first processed in the thalamus. The thalamus generates potentials that can be recorded from the scalp during intraoperative monitoring. Blood supply to the thalamus is from the posterior cerebral circulation making thalamic generated evoked potentials useful for monitoring posterior ischemia.

The Brainstem

The brainstem is composed of the midbrain, pons, and medulla oblongata and is continuous

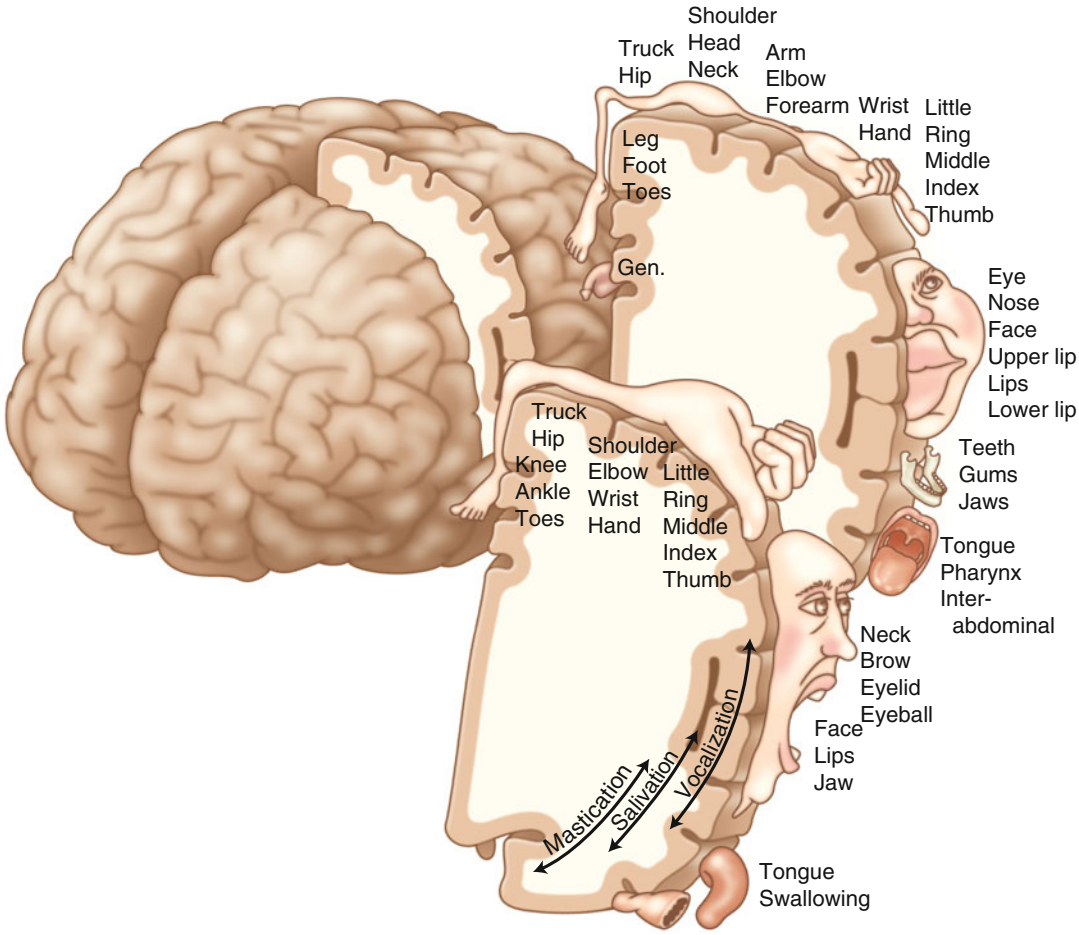

Fig. 2.15 Drawing of the motor and sensory homunculus. Notice that the face and upper extremity are represented laterally and the lower extremity and genitalia are represented medially

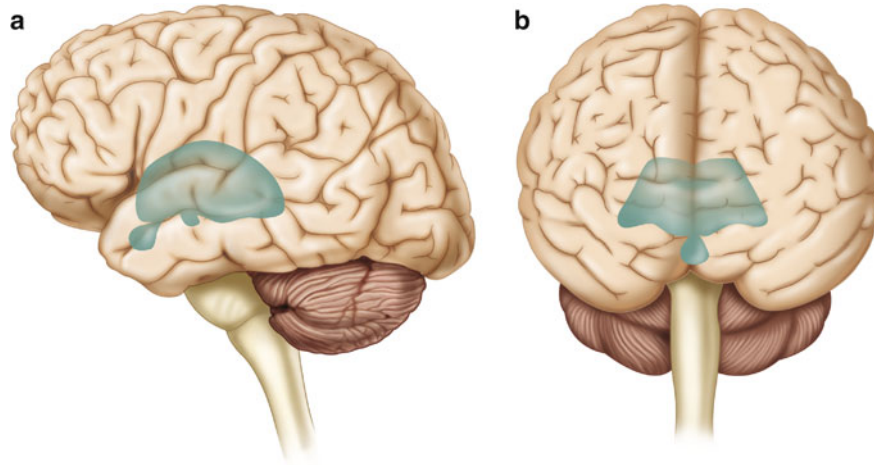

Fig. 2.16 Lateral (**a**) and anteroposterior (**b**) views of the diencephalon (*shaded*) within the neuraxis

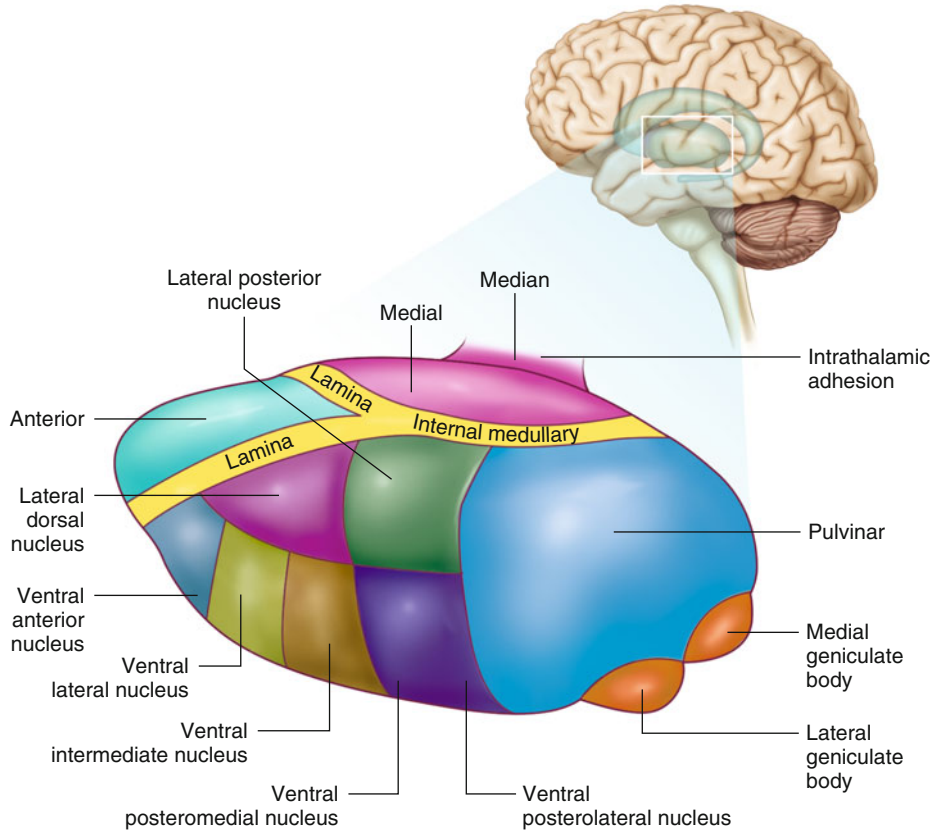

Fig. 2.17 Organization of the human thalamus

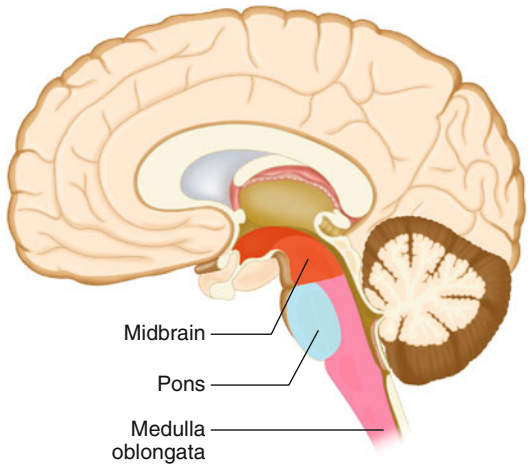

Fig. 2.18 Lateral view of the brainstem (midbrain, pons, and medulla oblongata) within the neuraxis

with the spinal cord (Fig. 2.18). The brainstem contains sensory and motor tracts passing information to and from the higher brain centers as well as cranial nerve nuclei. The cranial nerve nuclei contain the cell bodies whose axons form the cranial nerves, which supply sensory and motor innervation to the head, neck, and face. Vegetative functions are controlled by the brainstem including the heart rate, respiration, and aspects of the sleep–wake cycle. Intraoperative monitoring of various brainstem potentials can protect these vital structures and functions during surgery. We will discuss some of the brainstem structures in more detail in subsequent sections.

The Cranial Nerves

The cranial nerves emerge from the brain and innervate structures of the head and neck (Fig. 2.19). There are 12 cranial nerves that are motor, sensory, or mixed nerves. Some of the cranial nerves even have autonomic function, specifically parasympathetic function. Each nerve

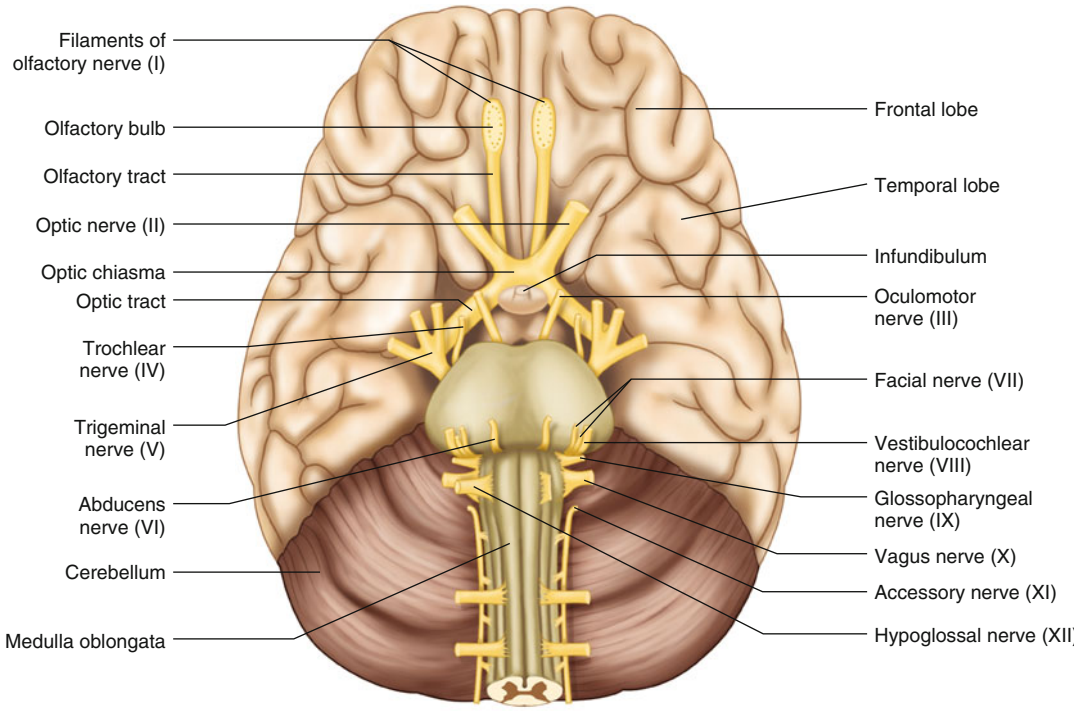

Fig. 2.19 Ventral view of the brain showing the 12 cranial nerves

has a unique name but may also be designated by its number. The numerical designation takes the form of "CN" followed by the Roman numeral assigned to the nerve. For example, the facial nerve is also designated CNVII. You should be familiar with both the names and numerical designations of all 12 cranial nerves.

Table 2.1 lists all of the cranial nerves as well as information about each nerve that you should know. There is only one cranial nerve that cannot be monitored and that is CNI, the olfactory nerve, which mediates the sense of smell.

Two of the sensory cranial nerves can be monitored by special evoked potentials. The optic nerve (CNII) and the visual pathway are monitored with visual evoked potentials (VEPs). VEPs are most often carried out in the clinic and are primarily used to diagnose optic neuritis and multiple sclerosis. Intraoperatively, VEPs are used to protect the optic nerve when there is a risk of damaging the nerve during a craniotomy, such as for removal of a tumor near the optic nerve or optic chiasm. Because VEPs are highly sensitive to anesthesia, reliable recordings are often difficult to obtain during surgery.

The vestibulocochlear nerve (CNVIII) is the other cranial nerve that is monitored with the use of special evoked potentials. CNVIII is actually two nerves in one (Fig. 2.20). The vestibular branch innervates the semicircular canals and is important for balance, while the auditory branch innervates the cochlea and mediates hearing. The auditory branch is monitored with the use of brainstem auditory evoked potentials (BAEPs). BAEPs are discussed in another chapter of this book.

Three cranial nerves innervate the extraocular muscles (Fig. 2.21). The oculomotor nerve (CNIII) controls most of the movements of the eye and also governs the pupillary reflex and accommodation. CNIII innervates all of the extraocular muscles except two. The ones innervated by CNIII are the superior rectus, medial rectus, and inferior rectus. A lesion of CNIII produces oculomotor palsy characterized by a lateral and downward deviation in the gaze known as

Table 2.1 The cranial nerves

Number	Name	Modality	Function	How monitored
I	Olfactory	Sensory	Smell	N/A
II	Optic	Sensory	Vision	VEP
III	Oculomotor	Motor	Eye movement, pupillary constriction	EMG from extraocular muscles (except trochlea and lateral rectus)
IV	Trochlear	Motor	Eye movement	EMG from superior oblique
V	Trigeminal	Both	Sensation to face, motor to muscles of mastication	EMG from masseter or temporalis
VI	Abducens	Motor	Eye movement	EMG from lateral rectus
VII	Facial	Both	Motor to muscles of facial expression, autonomic input to salivary glands, taste to anterior 2/3 of tongue	EMG from muscles of facial expression
VIII	Vestibulocochlear	Sensory	Hearing and balance	BAEP
IX	Glossopharyngeal	Both	Sensation to tonsils and pharynx, motor to stylopharyngeus, taste to posterior 2/3 of tongue, input to parotid gland	EMG from soft palate
X	Vagus	Both	Parasympathetic to thoracic and abdominal viscera, motor to vocal muscles	EMG from vocal cords (monitors recurrent laryngeal nerve)
XI	Spinal accessory	Motor	Motor to trapezius and sternocleidomastoid	EMG from trapezius
XII	Hypoglossal	Motor	Motor to tongue	EMG from tongue

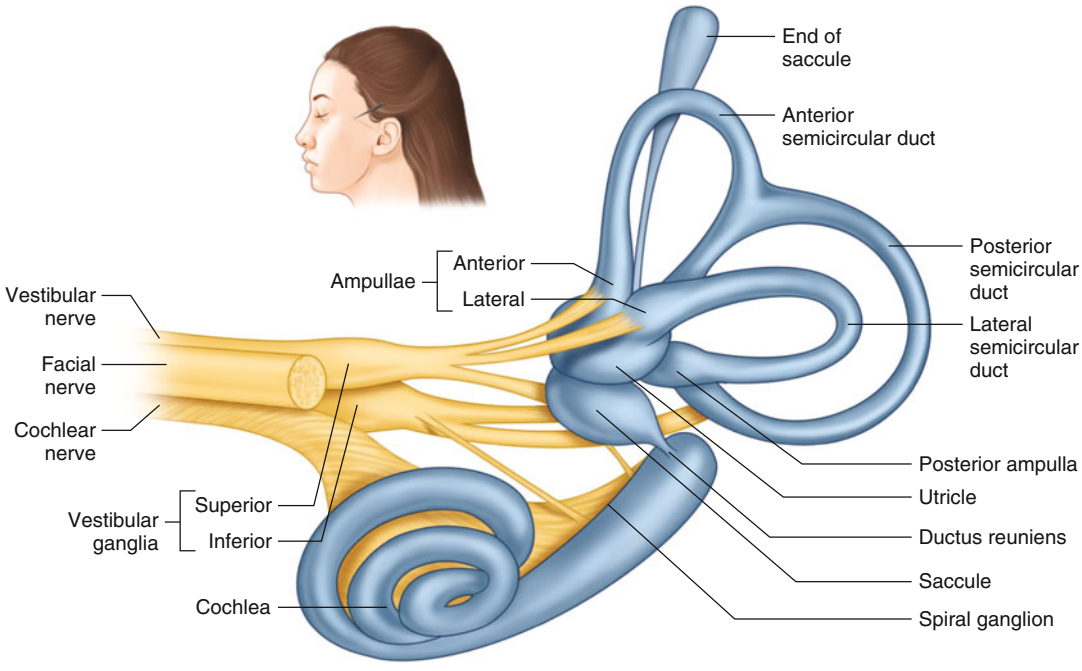

Fig. 2.20 The auditory and vestibular nerves emerge from the cochlea and semicircular canals, respectively, to form CNVIII. Note the association of the facial nerve as it travels with CNVIII through the temporal bone

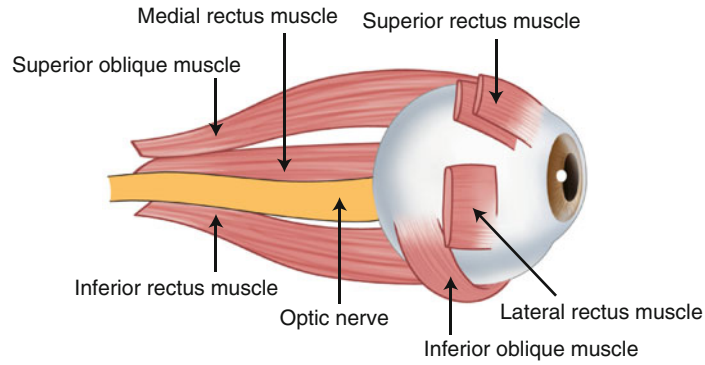

Fig. 2.21 The extraocular muscles

down and out symptoms. There are two remaining extraocular eye muscles that are innervated by other cranial nerves.

The trochlear nerve (CNIV) is a somatic motor nerve innervating the superior oblique muscle. The abducens nerve (CNVI) innervates the last remaining extraocular muscle, the lateral rectus. The easiest way to remember the innervation of CNVI is to look at its name, *abducens*. This word means to *abduct*, which is the term for movement away from midline. Movement away from midline is *lateral* movement. Therefore, the **abducens** nerve innervates the **lateral** rectus muscle.

The cranial nerves III, IV, and VI can be monitored with EMG from the appropriate extraocular muscles. It should be noted, however, that this requires special electrodes that are inserted with small needles and requires specialized training. For these reasons these nerves often go unmonitored.

Spontaneous and triggered EMG is used to monitor all the remaining cranial nerves. When possible it is advisable to electrically stimulate the nerve directly to confirm identification and function.

The trigeminal nerve (CNV) mediates sensation to the face as well as providing motor innervation to the muscles of mastication, namely, the temporalis and masseter. The trigeminal nerve has three branches: the ophthalmic nerve (V1), maxillary nerve (V2), and mandibular nerve (V3) (Fig. 2.22). The maxillary nerve (V3) has motor function and is monitored with EMG recorded from the masseter.

The facial nerve (CNVII) is one of the most complex of the cranial nerves as well as one of the most often monitored. It has general and special sensory function, parasympathetic function as well as motor innervation to the muscles of facial expression. The facial nerve mediates the sense of taste for the anterior two thirds of the tongue. Also, ironically, CNVII provides parasympathetic innervation to all of the salivary glands except the parotid, which it travels through.

Intraoperative monitoring of the facial nerve function is accomplished with spontaneous and triggered EMG from the muscles of facial expression (Fig. 2.23). There are five branches of the facial nerve (Table 2.2). The mnemonic **T**he **Z**ebra **B**it **M**y **C**ousin can be used to help remember the branches of the facial nerve temporal, zygomatic, buccal, marginal/mandibular, and cervical. It is worth adding that zebras are, in fact, vicious animals and should never be approached. If the intracranial portion of the facial nerve is at risk (such as during a posterior fossa craniotomy), then specific data concerning all branches is not necessary since this point is proximal to the point of branching. Surgery involving the parotid gland, which is at the point of nerve branching, necessitates monitoring all branches of the facial nerve. When equipment limitations compromise the ability to monitor all branches specifically, the marginal/mandibular branch becomes the highest priority to monitor because the fibers that contribute to this branch are located most superficially in the nerve.

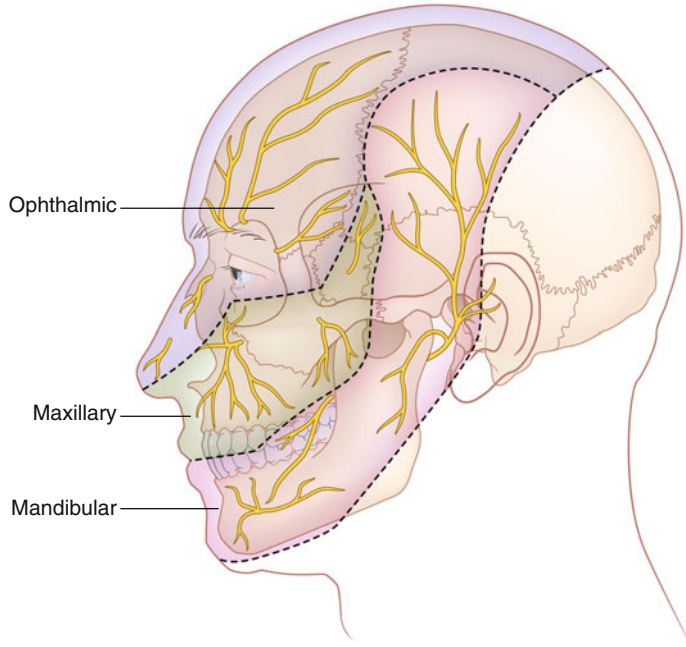

Fig. 2.22 The three branches of the trigeminal nerve and their sensory innervation of the face

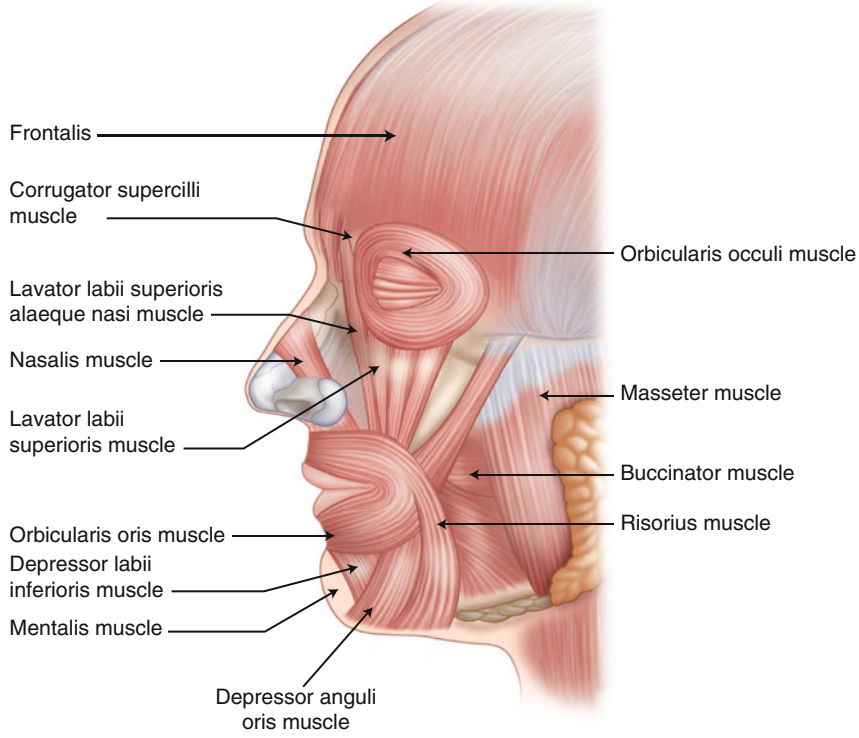

Fig. 2.23 Facial muscles

Table 2.2 Branches of the facial nerve

Branch	Mnemonic	Example muscle to monitor
Temporal	The	Orbicularis oculi
Zygomatic	Zebra	Nasalis
Buccal	Bit	Orbicularis oris
Marginal/mandibular	My	Mentalis
Cervical	Cousin	Platysma

The glossopharyngeal nerve (CNIX) is a mixed nerve that receives general sensory fibers from the pharynx, tonsils, and posterior one third of the tongue. Special sensory fibers mediating taste from the posterior one third of the tongue are likewise supplied by the glossopharyngeal nerve. This nerve has an autonomic component supplying parasympathetic innervation to the parotid gland. The only somatic motor component of the glossopharyngeal nerve is innervation to the stylopharyngeus muscle. We monitor CNIX by placing electrodes in the soft palate on the ipsilateral side which records far-field responses from the stylopharyngeus muscle.

The vagus nerve (CNX) is the largest parasympathetic nerve of the body. It innervates the thoracic and abdominal viscera, and its autonomic functions are not amenable to intraoperative monitoring. There are two motor branches of the vagus nerve, which supply the intrinsic laryngeal muscles. The superior laryngeal nerve innervates the cricothyroid muscle, while the recurrent laryngeal nerve (RLN) innervates most of the remaining laryngeal muscles. The RLN is so named because of the circuitous route it takes to its termination in the larynx (Fig. 2.24). The RLN branches from the vagus at high thoracic levels and then loops around the aortic arch (left) or subclavian artery (right) before ascending in the tracheoesophageal groove toward the larynx. The RLN is commonly monitored for anterior cervical fusion surgery, thyroidectomy, and sometimes during carotid endarterectomy. The RLN is also used to monitor the vagus nerve during a posterior fossa craniotomy, as it's the only branch of the vagus that can be monitored.

The spinal accessory nerve (CNXI) innervates two muscles of the neck, namely, the trapezius and sternocleidomastoid. The spinal accessory is purely a motor nerve. The last cranial nerve we will consider is also a motor nerve. The hypoglossal nerve (CNXII) provides motor innervation to the tongue and is important for aiding speech and swallowing. Placing electrodes in the ipsilateral side of the tongue is the method for monitoring the hypoglossal nerve.

Neurovasculature

An extensive network of blood vessels perfuses the brain. The neurovasculature can be divided into anterior and posterior circulations. A series of communicating arteries bridge the circulation from anterior to posterior as well as the left and right. These interconnecting vessels facilitate **collateral circulation** throughout the brain and collectively make up the structure known as **the circle of Willis** (Fig. 2.25). Collateral circulation is the flow of blood through alternate pathways when the main blood vessel is functionally impaired. People with good collateral flow are often able to tolerate ischemic events more readily than those without adequate collateral flow. Only a minority of humans have a complete circle of Willis. A majority have some variation of an incomplete circle of Willis. An understanding of brain perfusion is essential to the neuromonitoring clinician, as you will be called upon to correlate changes in electrical potentials to the anatomic location and the blood supply in order to make accurate real-time interpretations of your data.

The anterior circulation is supplied by the paired internal carotid arteries (ICA) and is responsible for perfusion of the majority of the cerebral cortex (Fig. 2.26). The right and left internal carotids enter the base of the brain and bifurcate into the middle cerebral artery (MCA) and anterior cerebral artery (ACA). The MCA supplies the lateral aspects of the cerebral hemispheres including the hand and face areas of the sensory and motor homunculi. The vascular territory of the ACA includes the medial most aspects of the cerebral hemispheres including areas of the sensory and motor homunculi that represent the lower extremity and genitalia.

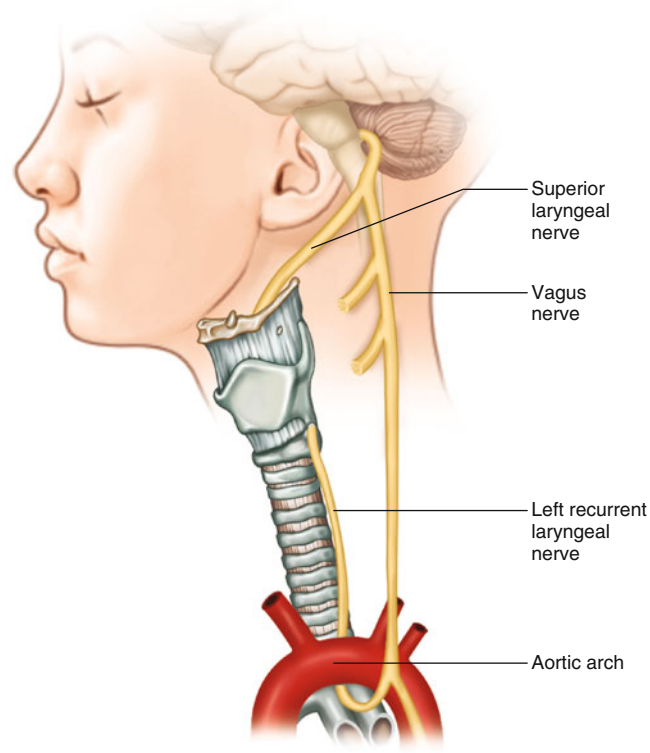

Fig. 2.24 The vagus nerve and its laryngeal branches: recurrent and superior laryngeal nerves

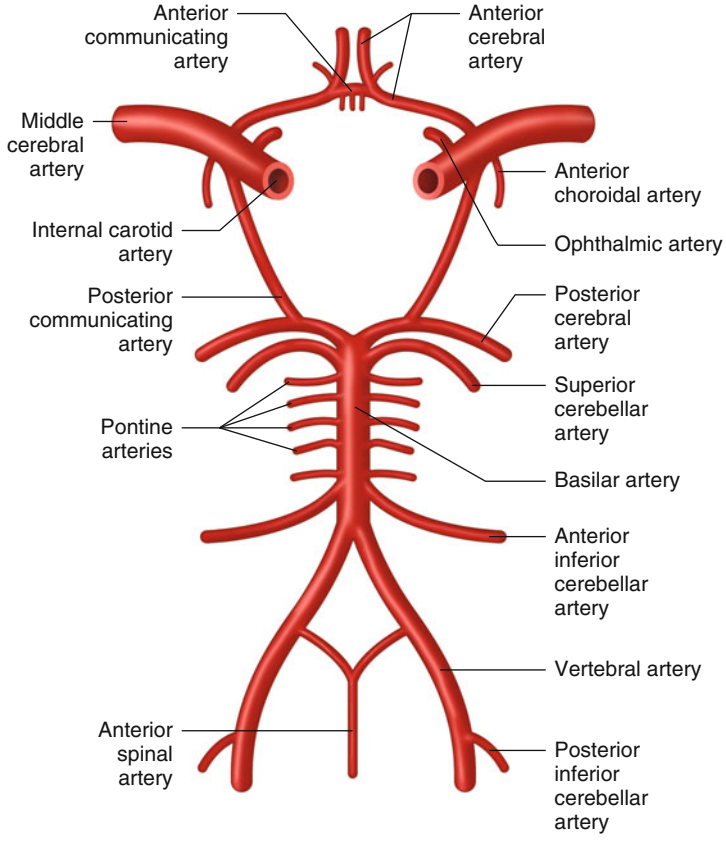

Fig. 2.25 The circle of Willis

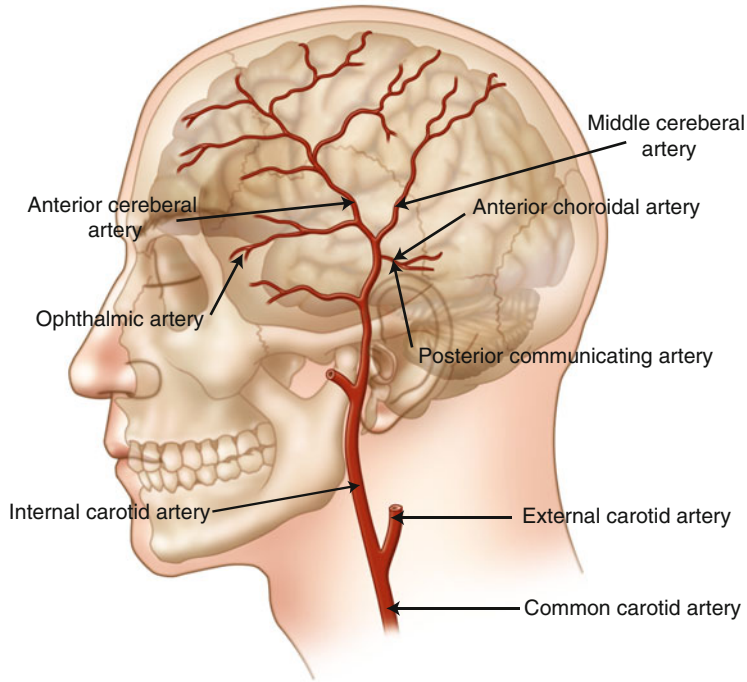

Fig. 2.26 Anterior cerebral circulation

The left and right anterior circulations are connected via the anterior communicating artery.

A lesion in the vascular territory of the MCA will result in sensorimotor deficits in the contralateral face and upper extremity. The deficits are contralateral because the sensory and motor pathways affected are crossed pathways. We will discuss this in greater detail below. An ACA territory lesion results in sensorimotor deficits in the contralateral lower extremity. These cerebral functional areas are best monitored by the upper and lower extremity sensory and motor evoked potentials.

Cerebral areas supplied by overlapping terminal branches of both the MCA and ACA are known as watershed areas. These areas have reduced blood flow compared to the rest of the vascular territory and, as such, are more vulnerable to reductions in blood flow. The watershed areas are the most frequent site of stroke, comprising approximately 10 % of all strokes. Strokes in this area are termed **watershed infarcts**.

The posterior circulation is supplied by the vertebrobasilar complex consisting of the vertebral and basilar arteries and their branches (Fig. 2.27). The posterior circulation supplies the occipital lobes of the brain, subcortical structures such as the thalamus, as well as the brainstem and cerebellum. A pair of vertebral arteries arising from the subclavian arteries ascends through the transverse foramina of the cervical vertebrae before joining at midline to form the basilar artery. The anterior spinal artery is given off from the vertebral arteries and supplies the anterior two thirds of the spinal cord. There is only one anterior spinal artery, but it receives contributions from both the left and right vertebral arteries.

The largest branch of the vertebral artery is the posterior inferior cerebellar artery (PICA), which is one of the three main blood vessels supplying the cerebellum. The two other main cerebellar arteries are the anterior inferior cerebellar artery (AICA) and the superior cerebellar artery (SCA), both are branches of the basilar artery. Branching

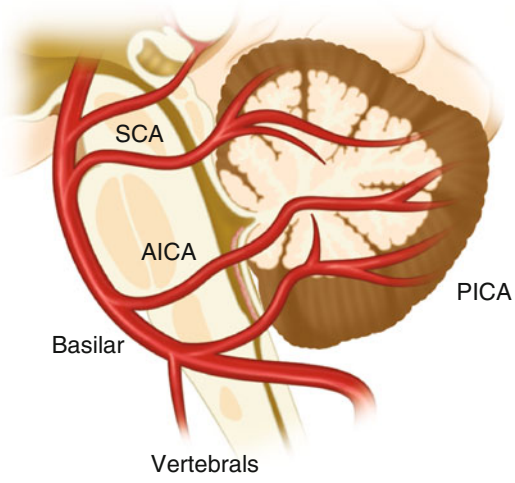

Fig. 2.27 Lateral view of the brainstem and cerebellum illustrating the posterior circulation. *SCA* superior cerebellar artery, *PICA* posterior inferior cerebellar artery, *AICA* anterior inferior cerebellar artery

from the left and right PICA are the two posterior spinal arteries, which supply the posterior one third of the spinal cord. Together with the anterior spinal artery mentioned above, these arteries contribute significantly to spinal cord perfusion (Fig. 2.28). We will discuss some additional features of spinal cord perfusion in "The Spinal Cord" section of this chapter.

The labyrinthine artery is an important branch of AICA providing blood to the cochlea. Compromise of the labyrinthine artery results in a cochlear stroke and loss of hearing as well as all waves of the brainstem auditory evoked potential.

The basilar artery terminates into the left and right posterior cerebral arteries, which supply blood to the occipital lobes, medial aspects of the temporal lobes, and the midbrain. Two posterior communicating arteries arise from the posterior cerebral artery and provide a connection to the anterior circulation thus completing the circle of Willis.

Deficits resulting from lesions of the vertebrobasilar system range from cranial nerve palsies and autonomic dystonia to sensorimotor symptoms such as quadriparesis. Intraoperative monitoring changes that may indicate posterior ischemia include critical changes in brainstem auditory evoked potentials, motor evoked potentials, or somatosensory evoked potentials. Thalamic and brainstem-generated potentials are particularly likely to be reduced in amplitude.

The Spinal Column

The spinal column provides protection of the spinal cord and allows for movement of the torso. Made up of 33 bones, called vertebrae, the spine is both incredibly protective and flexible. The spinal column is divided into segments. The cervical, thoracic, and lumbar segments are comprised of individual vertebra separated by intervertebral discs allowing for movement. The sacral and coccygeal segments of the spinal column are comprised of fused vertebrae and are immobile. Of the 33 total vertebrae, 7 are cervical, 12 thoracic, 5 lumbar, 5 fused sacral, and 4 fused coccygeal (Fig. 2.29). Most of the vertebrae contain a **body** sometimes called the centrum. A **vertebral arch** formed by the left and right **pedicles** and a **lamina** enclose a space known as the **vertebral canal**, also called the spinal canal. The vertebral canal contains the spinal cord or nerve roots depending on the level.

Curvatures of the Spine

In a normal spine there are curvatures, which are important for helping the spine perform its functions of providing balance, movement, and the distribution of loads. Cervical and lumbar concavities are termed lordosis, while thoracic and sacral convexities are termed kyphosis (Fig. 2.30). During fetal development and for a period of time during infancy, the spine is curved in a "C" shape, which is kyphotic. The secondary lordotic curves develop as the child begins to hold his head up and eventually walk and is a result of increased musculature and increased load bearing on the spine. The cervical lordosis and thoracic kyphosis have a normal range of between 20 and 40°, and the lumbar lordosis ranges from 40 to 60°. Curvatures in excess of this range are considered abnormal, and the patient is then said to be "kyphotic" or "lordotic."

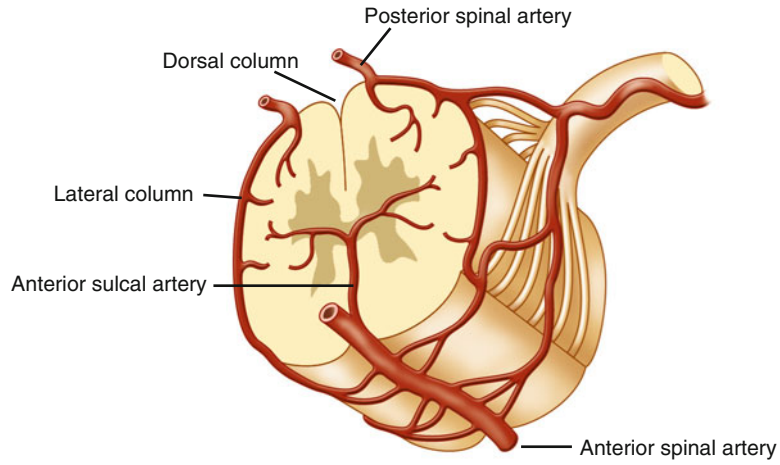

Fig. 2.28 Spinal cord arterial circulation

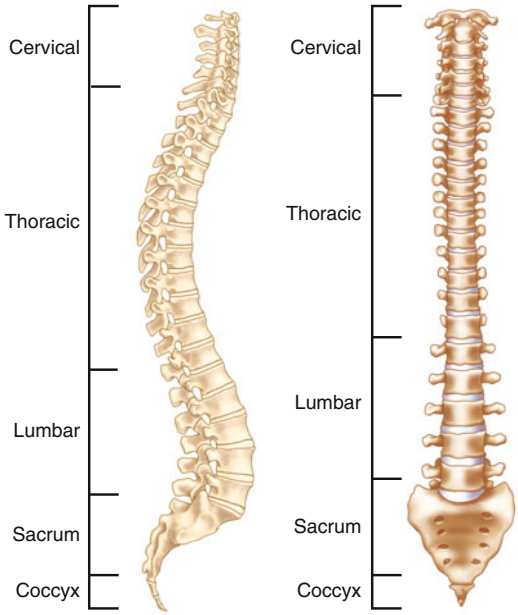

Fig. 2.29 Lateral and posterior view of the vertebral column and its divisions

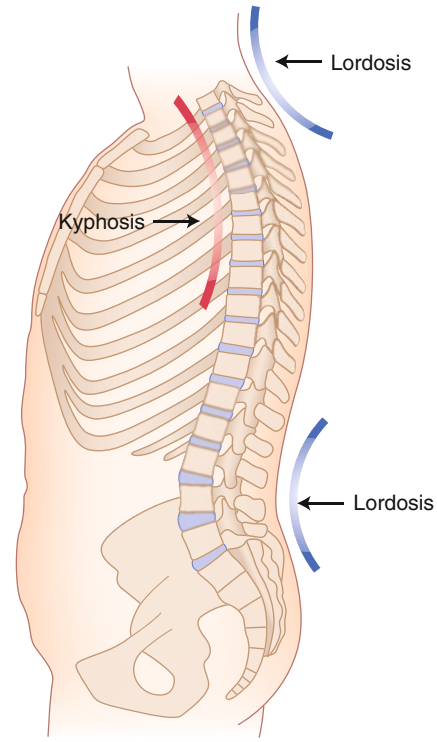

Fig. 2.30 Normal curvatures of the spine

An abnormal lateral curvature of the spine (greater than 10°) is known as scoliosis (Fig. 2.31). Scoliosis can either be idiopathic, having no known cause, or a result of a neuromuscular disease. Most cases of scoliosis are idiopathic. Neuromuscular scoliosis may be part of a larger syndrome that involves other body systems. Scoliosis tends to progress as a child ages and can begin to interfere with the vital capacity, the ability to breathe. Surgical intervention is often required for spinal deformities such as scoliosis. The outcomes for spinal deformity surgery have improved since the advent of intraoperative neurophysiologic monitoring.

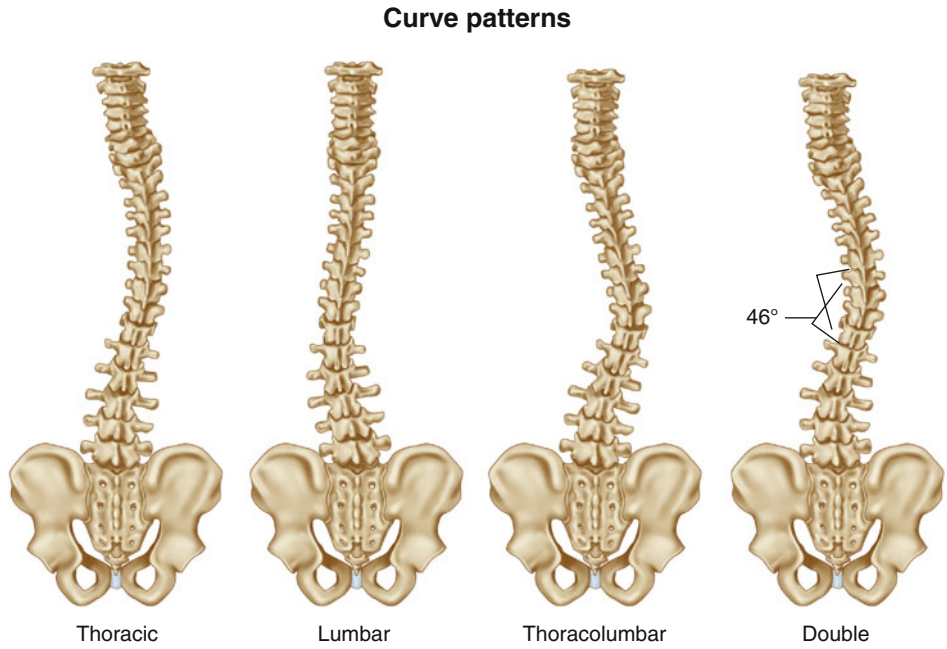

Fig. 2.31 Commonly seen curve patterns in patients with scoliosis

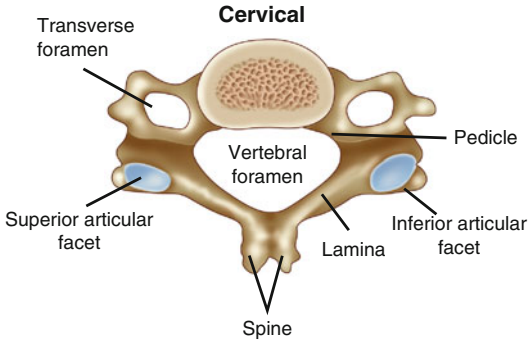

Fig. 2.32 A typical cervical vertebra seen between C3 and C6

Cervical Vertebrae

The cervical vertebrae are the smallest of all the vertebral types and allow for maximal movement. The cervical vertebrae are distinguished by some unique characteristics common to C3–C6 (Fig. 2.32). There are three distinct cervical vertebrae: C1, C2, and C7 which we will consider separately.

General Characteristics of C3–C6

In addition to their small and flattened bodies, each cervical vertebra has a pair of foramina located in the transverse processes. These **transverse foramina** contain the vertebral artery, vein, and sympathetic nerve plexus. The spinous processes of these vertebrae are bifid with one side usually larger than the other. The pedicles of the cervical vertebrae are small and project posterolaterally. The vertebral canal contains the spinal cord, while the intervertebral foramen, formed by the articulation of two vertebrae, is the exit point for the spinal nerves.

Special Cervical Vertebrae (C1, C2, and C7)

The C1 vertebra has the name **atlas** after the Greek mythological god that carried the world on his shoulders. You may therefore guess that atlas joins the skull with the spine. The atlas has no body but rather is a ring consisting of an anterior and posterior arch. C1 fuses with the body of C2, the axis (Fig. 2.33a).

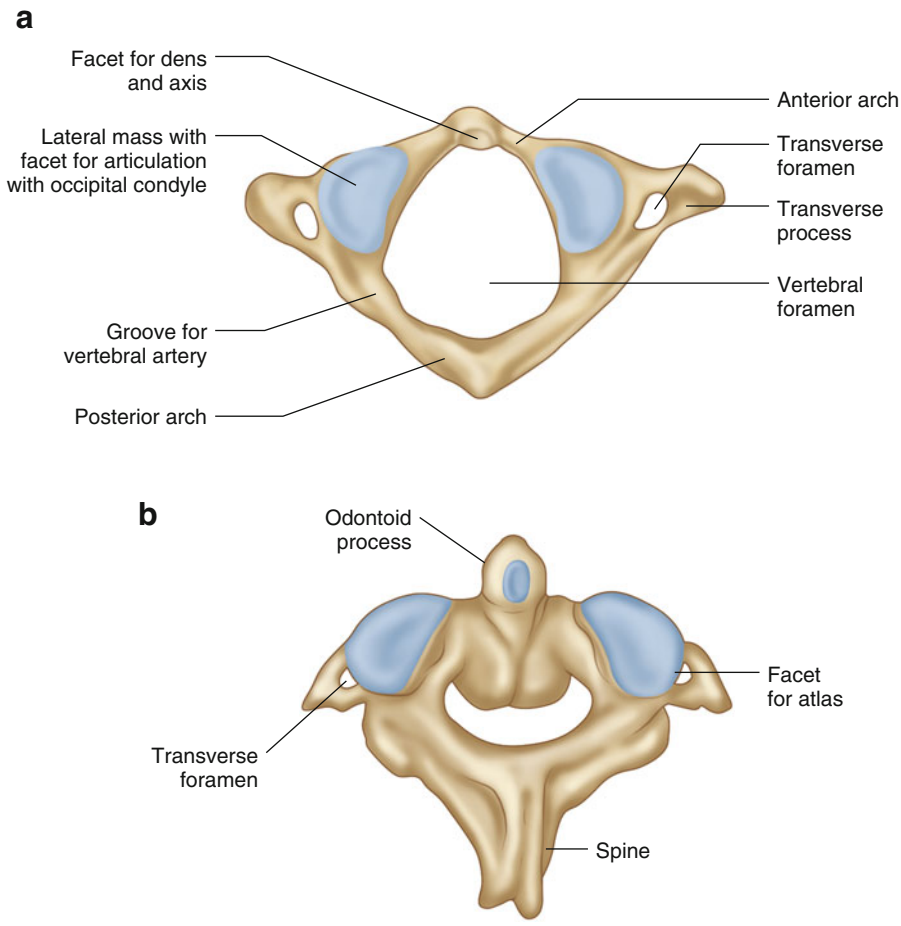

Fig. 2.33 (**a**) The C1 vertebra, atlas. (**b**) The C2 vertebra, axis

The C2 vertebra is named **axis** for the fact that it provides an axis of rotation for C1. Its most prominent feature is the bony projection known as the dens. The dens is also called the odontoid process, since it resembles a tooth (Fig. 2.33b). The union between C1 and the occiput is the atlanto-occipital joint which is responsible for the nodding movement of the head. The C1–C2 joint is also known as the atlanto-axial joint and provides for rotation of the head on the neck.

The C7 vertebra has a prominent spinous process and therefore is named **vertebra prominens**. Occasionally C7 has an abnormal pair of ribs associated with it that can cause compression of blood vessels as well as the nerves of the brachial plexus. This condition, known as **thoracic outlet syndrome**, can cause pain, numbness, and tingling in the upper extremity.

Thoracic Vertebrae

The thoracic segment of the vertebral column is the least flexible due to the attachment of the ribs. The ribs attach to facets located both on the vertebral body and the transverse processes. These facets are called **costal facets**. The bodies of the thoracic vertebrae are larger than the cervical but smaller than the lumbar (Fig. 2.34). The size increases with progression from T1 to T12. The vertebral canal contains the spinal cord, and the intervertebral foramina remain the exit points for the spinal nerves.

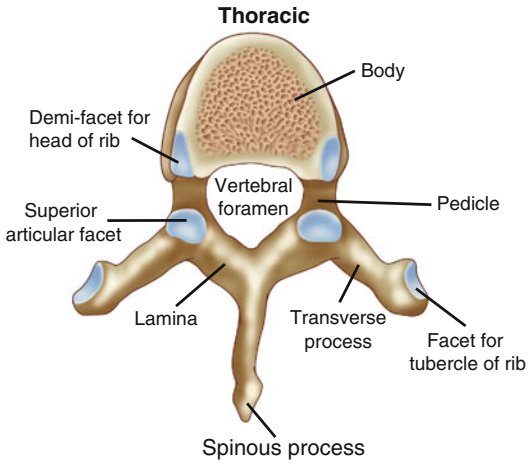

Fig. 2.34 A typical thoracic vertebra

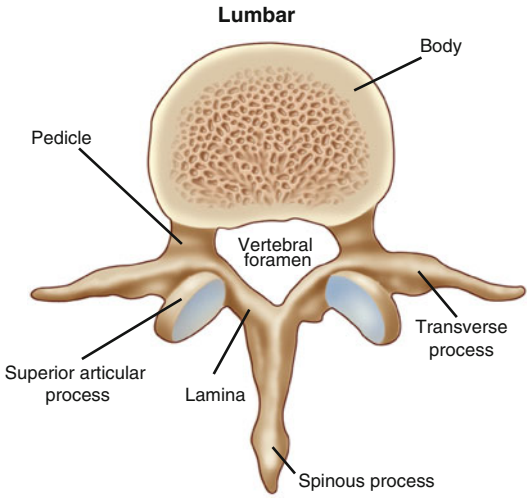

Fig. 2.35 A typical lumbar vertebra

Lumbar Vertebrae

The five lumbar vertebrae are the largest in size and are characterized by the absence of both transverse foramina and costal facets (Fig. 2.35). The spinal cord usually ends at vertebral level L1. At levels caudal to L1, the lumbar and sacral nerve roots occupy the vertebral canal as they descend toward their respective vertebral levels to exit. At the most rostral lumbar segments, there are more nerve roots occupying the vertebral canal. As you progress toward L5 the number of nerve roots in the canal diminishes as they begin to exit the vertebral column (Fig. 2.36). The lumbar region of the spine is highly mobile and is responsible for bearing the most compressive load. For this reason, the lumbar region is also the most vulnerable to injury. Of all of the lumbar vertebrae, L5 is the most common site of injury and disease.

The Sacrum and Coccyx

The **sacrum** is a large triangular shaped bone that is comprised of five fused sacral vertebrae. The sacrum fits like a wedge in between the two hipbones of the pelvis. Inferior to the sacrum is the **coccyx** or tailbone, which is comprised of four fused coccygeal vertebrae.

The Spinal Cord

The spinal cord is part of the central nervous system extending from termination of the medulla oblongata to approximately the L1 vertebral level. The function of the spinal cord is to transmit sensory and motor information to and from the brain and periphery. Like the vertebral column, the spinal cord is divided into cervical, thoracic, lumbar, sacral, and coccygeal levels. The cervical cord is divided into eight segments even though there are only seven cervical vertebrae. There are 12 thoracic segments, 5 lumbar segments, 5 sacral segments, and 1 coccygeal segment. Each spinal cord segment gives rise to a pair of spinal nerves for a total of 31 pair of spinal nerves.

The spinal cord is larger in diameter at the cervical and lumbar levels due to the increased number of cell bodies and nerve fibers dedicated to the innervation of the limbs. These areas are known as the **cervical and lumbar enlargements** (Fig. 2.37).

The spinal cord is contained within the dural sac, often called the **thecal sac**, and is bathed by cerebral spinal fluid. The spinal cord is anchored at its caudal end to the thecal sac by an extension

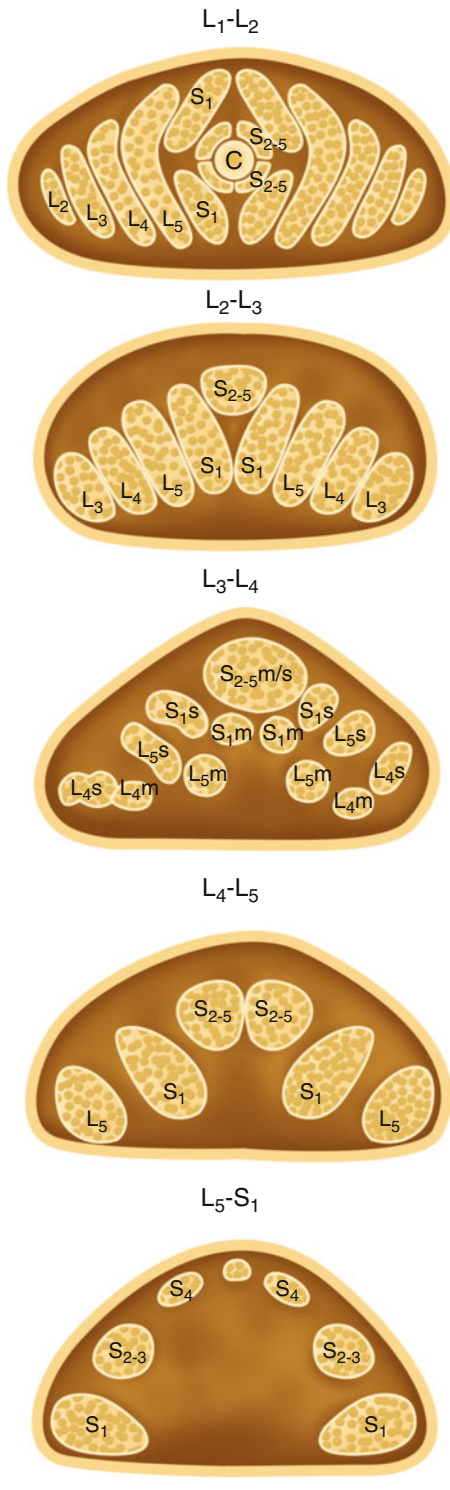

Fig. 2.36 Serial cross sections through the cauda equina showing the decreasing number of nerve roots remaining as you approach lower lumbar and sacral vertebral levels

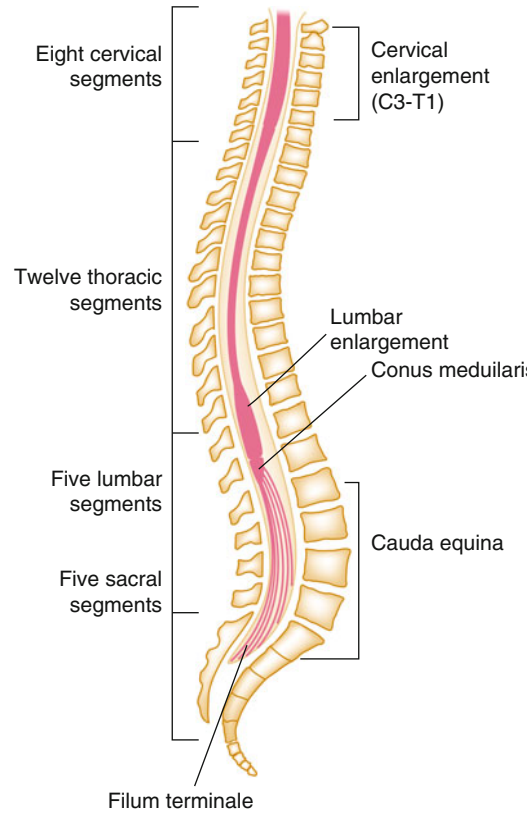

Fig. 2.37 The spinal cord showing the lumbar and cervical enlargements, conus medullaris, and filum terminale

of the pia mater called the **filum terminale** (Fig. 2.37). The filum terminale internum anchors the spinal cord to the interior surface of the dural sac. The filum terminale externum is the continuation of the filum internum, which anchors the dural sac to the coccyx.

The spinal cord ends at about the L1 vertebral level in a tapered structure known as the **conus medullaris** (Fig. 2.37). The conus medullaris contains the lower lumbar and sacral spinal cord segments. Surgery near the L1 vertebral level, therefore, places sacral function at risk due to the proximity of the conus. For this reason, the external anal sphincter should be monitored for procedures at T12 or L1 vertebral levels. Injury to the conus medullaris will result in nerve palsies of the lumbosacral plexus including deficits in bowel and bladder control. Sexual function may also be compromised.

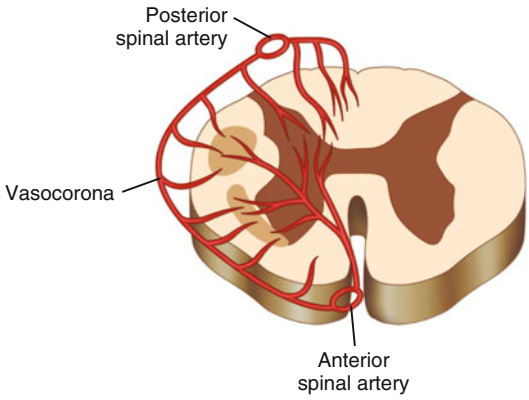

Fig. 2.38 The vasocorona is an anastomosis between the anterior and posterior spinal arteries

Spinal Cord Vasculature

Three longitudinal arteries arising from the posterior cerebrovasculature (as discussed above) perfuse the spinal cord. There is collateral circulation among these three arteries via anastomoses. These anastomoses form the **vasocorona** (Fig. 2.38). In addition to the three longitudinal arteries, each spinal cord level is fed by the anterior and posterior radicular arteries, which enter the cord along the nerve roots. The word *radicular* means nerve root. The radicular arteries have anastomoses with each other providing collateral flow. The anterior radicular arteries contribute to the vascular territory of the anterior spinal artery, and the posterior radicular arteries contribute to the vascular territory of the two posterior spinal arteries. The largest anterior radicular artery is known as the **artery of Adamkiewicz** (Fig. 2.39). This artery is highly variable and in most people arises from the aorta on the left side at low thoracic or high lumbar vertebral segments. This artery bolsters the perfusion of the anterior two thirds of the lumbar and sacral segments of the spinal cord. The artery of Adamkiewicz may be placed at risk during surgical procedures of the lower thoracic region, especially those that utilize a lateral approach or involve interruption of the radicular blood supply. Provocative testing with motor evoked potentials is used to monitor perfusion of the spinal cord and help determine whether a particular radicular vessel can be sacrificed or temporarily clamped.

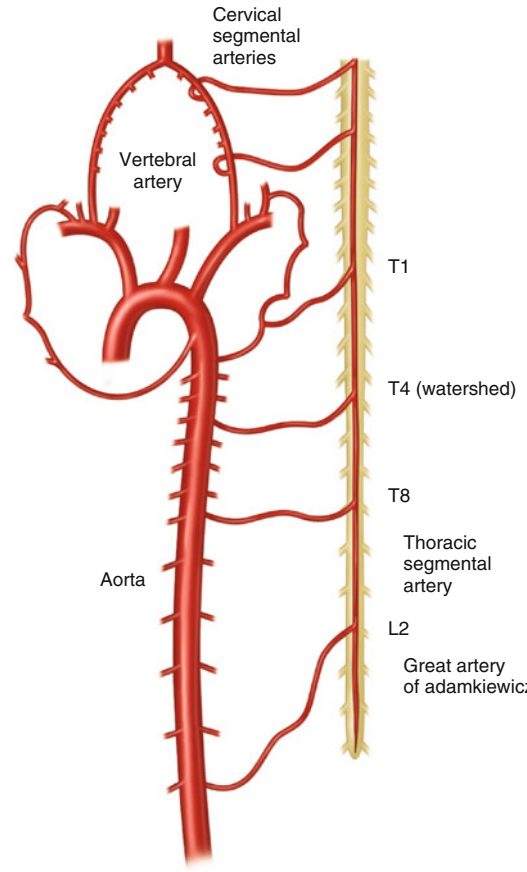

Fig. 2.39 Segmental arteries coming off of the aorta. The artery of Adamkiewicz is shown emerging from the aorta adjacent to the upper lumbar spinal cord segments

Internal Organization of the Spinal Cord

A cross section through the human spinal cord reveals white matter in the periphery surrounding a butterfly-shaped gray matter in the center. A central canal continuous with the ventricles of the brain contains CSF. Figure 2.40 illustrates the white matter organization of the spinal cord. The gray matter is organized into ten functional layers known as Rexed's laminae (Fig. 2.41).

There are several areas of particular importance to the neuromonitoring clinician. The dorsal columns carry specific sensory information from the periphery to the brain. As we will discuss below, the dorsal columns are further divided into

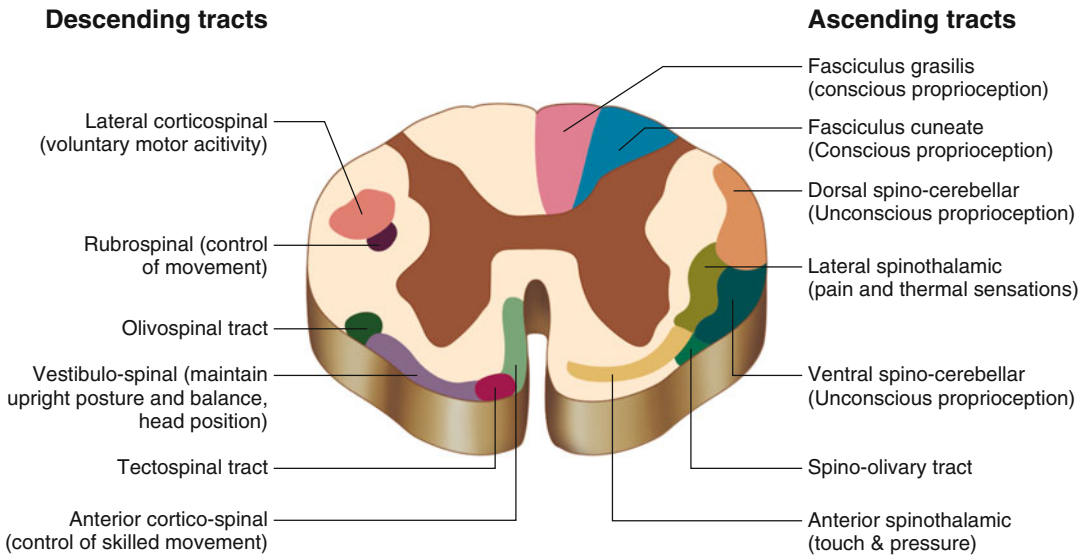

Fig. 2.40 A cross section through the spinal cord showing the white matter organization. Descending tracts (motor) are illustrated on the *left*, while ascending tracts (sensory) are illustrated on the *right*

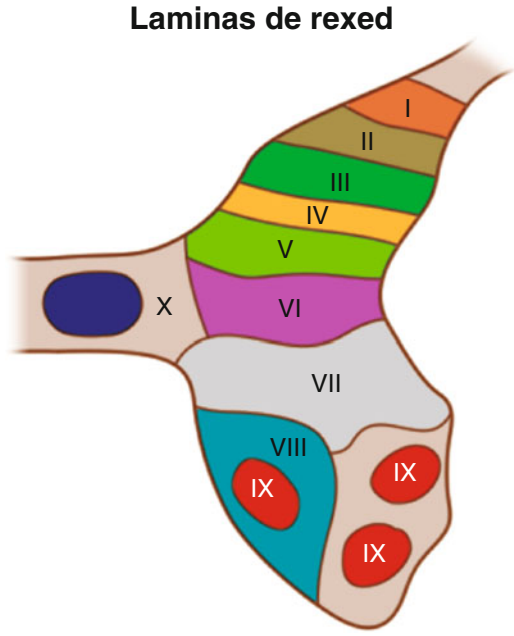

Fig. 2.41 Organization of the spinal cord gray matter into Rexed's laminae

smaller white matter tracts or **fasciculi**. The dorsal columns are part of the dorsal column medial lemniscal pathway that is monitored with somatosensory evoked potentials. Another important area of white matter is the corticospinal tract which is responsible for voluntary movement and is monitored using motor evoked potentials.

Rexed's laminae IX and X contain neuronal cell bodies that are also part of the corticospinal tract. These neurons are contained within the ventral portion of the spinal cord gray matter, an area often called the **ventral horn**.

Spinal Nerves

Each segment of the spinal cord gives rise to a pair of spinal nerves, 31 total. Each spinal nerve is a mixed nerve comprised of a dorsal (sensory) root and ventral (motor) root (Fig. 2.42).

The dorsal root brings sensory information from the periphery into the spinal cord. Neurons that make up the dorsal root have their cell body located in a structure known as the dorsal root ganglion (DRG). There are paired DRG at each spinal cord segment. Neurons of the DRG are of the pseudounipolar morphological type. Pseudounipolar neurons have one process that bifurcates into two: a central and peripheral process. The peripheral process terminates in a peripheral target and has a sensory receptor at its

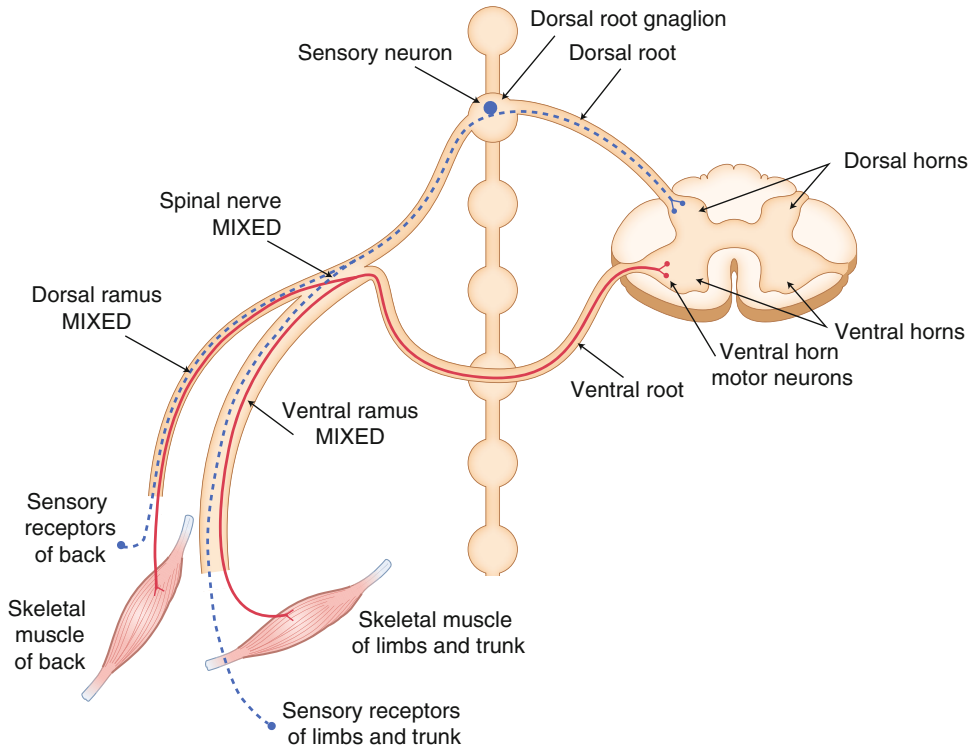

Fig. 2.42 Organization of spinal nerves

ending. The sensory receptor recognizes specific sensory modalities. The central process of neurons in the DRG enters the spinal cord through the dorsal root.

The ventral root of the spinal nerve carries motor information from the spinal cord to the periphery. Neurons located in the ventral horn send their axons out via the ventral root. The dorsal and ventral roots join to form the spinal nerve before exiting the vertebral column via the intravertebral foramen. Monitoring the nerve roots during surgery is one of the functions of IOM. The dorsal root has been monitored using dermatomal SSEPs, but this technique has been largely replaced by using EMG to monitor the ventral roots.

Neural Pathways

The function of the nervous system can be monitored intraoperatively by stimulating and recording from opposite ends of neural pathways. Stimulating sensory pathways distally and motor pathways proximally while recording from the opposite ends can determine the integrity of an entire neural pathway.

In order to both design the monitoring plan and accurately interpret the data, the monitoring clinician must have a detailed understanding of the neural pathway being tested. We will discuss two pathways in this section: the **dorsal column medial lemniscal tract** (DCML) and the **corticospinal tract** (CST). It is critical that IOM clinicians be familiar with both of these pathways. There are many other neural pathways that are not directly tested with IOM techniques, and as such they will not be considered in this volume.

DCML Pathway

The DCML pathway is a sensory pathway mediating the sensory modalities of deep touch, vibration, conscious proprioception, two-point discrimination, and stereognosis (recognition of texture). Occupying part of the dorsal white

matter of the spinal cord, this pathway lies in the vascular territory of the posterior spinal arteries. The DCML pathway is monitored using SSEPs as a means of protecting the spinal cord during surgery. A detailed knowledge of the DCML pathway is required for accurate monitoring of SSEP data during surgery.

There are three neurons of the DCML pathway. The first-order neuron has its cell body in the dorsal root ganglion. Sensory information encoded by specialized nerve endings moves along the peripheral process of the first-order neuron and then to the spinal cord via the central process traveling with other fibers of the dorsal root of the spinal nerve.

The medial division of the dorsal columns is called the **fasciculus gracilis**. The fasciculus gracilis carries information entering the spinal cord from the lower thoracic, lumbar, and sacral spinal nerves. Sensory information from the upper thoracic and cervical regions enter the spinal cord and ascend in the **fasciculus cuneatus**, the lateral division of the dorsal columns. There is a medial to lateral topography of the dorsal columns with sensory information from the lower extremity medial and the upper extremity lateral. This is similar to the homuncular organization of the primary somatosensory cortex.

The axons of the dorsal columns continue to ascend in the spinal cord without synapsing until they reach the caudal medulla and synapse in the **dorsal column nuclei**. There are two pairs of dorsal column nuclei: nucleus gracilis and nucleus cuneatus. The dorsal column nuclei contain the cell bodies of the second-order neurons of the DCML pathway. Fibers from the fasciculus gracilis synapse in the nucleus gracilis, while fibers traveling in the nucleus cuneatus synapse in the nucleus cuneatus.

The second-order neurons of the dorsal column nuclei send their axons, named **internal arcuate fibers**, out and across midline to ascend in the brainstem as a white matter tract called the **medial lemniscus**. The crossing over of white matter tracts is called a decussation. The fibers of the DCML pathway cross at a point called the **sensory decussation**. The medial lemniscus now contains fibers from the contralateral side of the body. The medial lemniscus ascends through the pons and midbrain on its way to the thalamus, where its fibers will synapse on the third-order neurons of the DCML pathway.

The thalamus is a multinucleated deep brain structure that relays sensory information from the periphery to the cortex. The nucleus of the thalamus that receives input from the DCML pathway is the ventroposterolateral nucleus of the thalamus (VPL). Fibers of the medial lemniscus terminate in the VPL on the third-order neurons of the DCML pathway. Axons leaving the VPL ascend through the internal capsule and are known as the **thalamic radiations**. These fibers next synapse in the primary somatosensory cortex located on the postcentral gyrus. Axons carrying sensory information from the lower extremity synapse more medially than axons carrying information from the upper extremities. The DCML pathway is shown in detail in Fig. 2.43.

Corticospinal Tract

The **corticospinal tract** is a motor pathway that mediates voluntary movement of the limbs and trunk, often called the **pyramidal tract** because its fibers create surface features in the medulla known as the pyramids. There are two neurons in this pathway: an **upper motor neuron** and a **lower motor neuron** (Fig. 2.44). The upper motor neuron resides in layer V of the primary motor cortex located in the precentral gyrus. You should recall the homuncular organization of the precentral gyrus. The lower motor neuron, also called the alpha motor neuron, is located in the ventral horn of the spinal cord gray matter.

Voluntary motor control is initiated at the level of the upper motor neuron. Axons of the upper motor neurons pass through the internal capsule and descend through the midbrain and pons before reaching the medulla. In the caudal medulla, approximately 80 % of the fibers decussate in an area known as the pyramidal or motor decussation. The crossed fibers and a small percentage of the uncrossed fibers contribute as the lateral corticospinal tract and synapse on lower

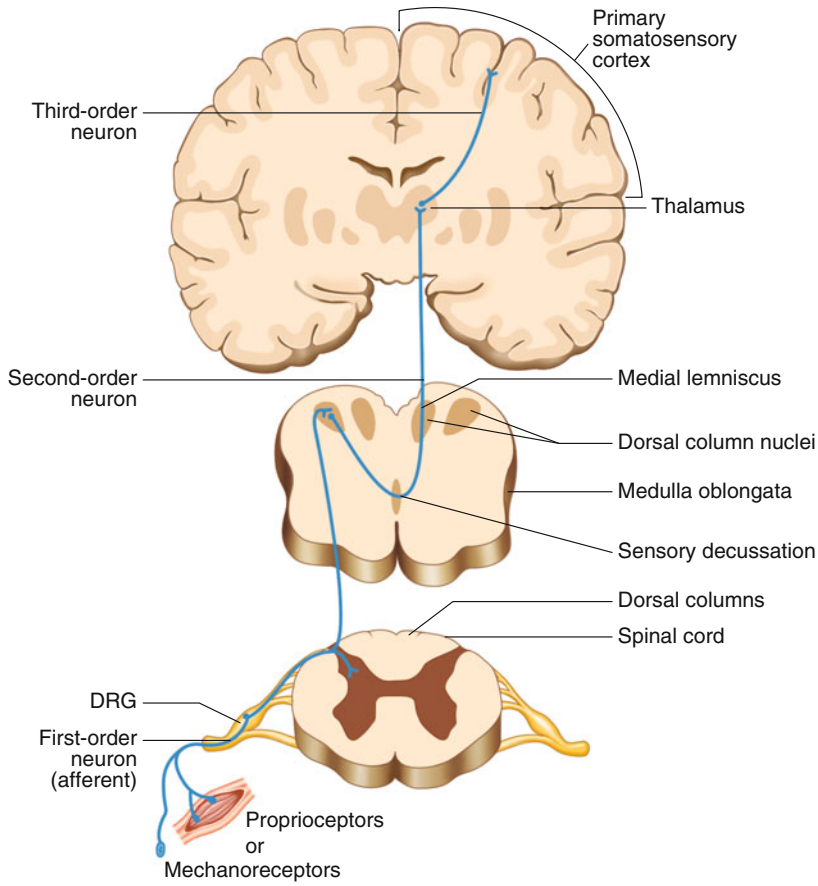

Fig. 2.43 The dorsal column medial lemniscal (DCML) pathway

motor neurons that innervate distal musculature. Most of the fibers that remain uncrossed at the level of the pyramidal decussation continue as the anterior corticospinal tract. These fibers generally cross near the level where they synapse. They synapse on lower motor neurons that innervate the proximal musculature.

The lower motor neurons are tonically inhibited by both descending inputs and afferent input from the musculature. Such tonic inhibition provides a mechanism for control over the skeletal muscles. Descending inputs from the upper motor neurons of the CST synapse on the alpha motor neurons and, if the input is sufficient, bring them to threshold causing an action potential. These action potentials travel along axons running in the ventral root and join the spinal nerve and peripheral nerves on their way to the target skeletal muscle.

Nerve Plexuses

A nerve plexus is an interconnecting group of nerves, innervating the same area of the body. Branches of a nerve plexus may join to become one or more larger peripheral nerves. The somatic peripheral nervous system contains the cervical, brachial, lumbar, and sacral plexuses. Intraoperative monitoring clinicians will encounter the brachial, lumbar, and sacral plexuses most often in their practice.

Brachial Plexus

The brachial plexus is a network of interconnecting ventral rami from spinal nerves C5–T1 that innervates the arm, forearm, and hand.

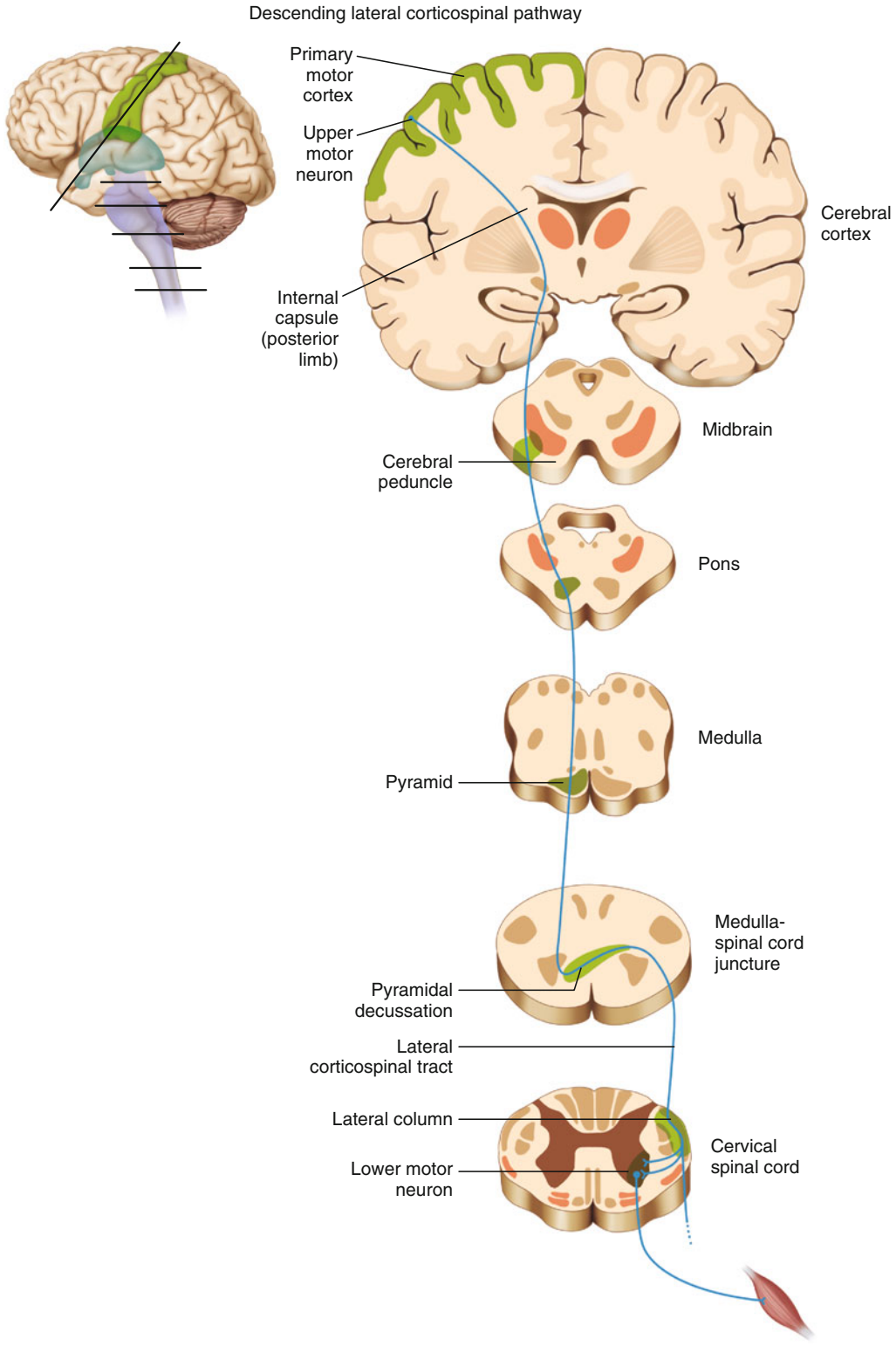

Fig. 2.44 The corticospinal tract

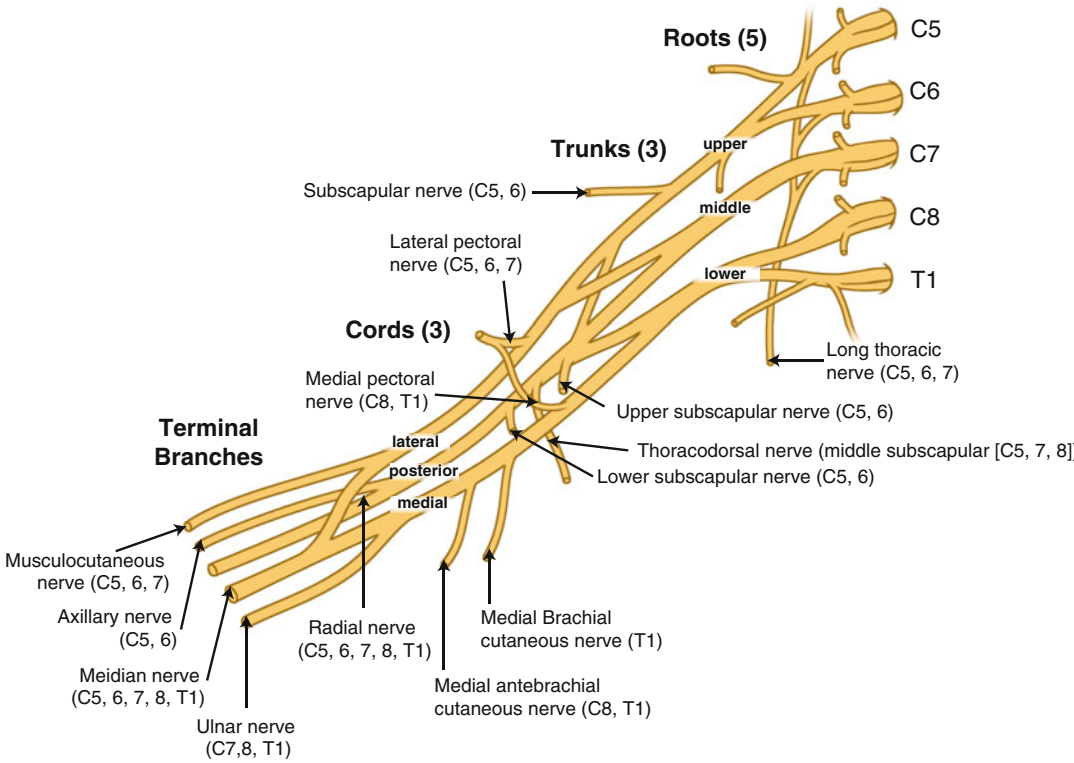

Fig. 2.45 The brachial plexus

Note: The term ventral ramus is not synonymous with the term ventral root! After the dorsal and ventral roots join to form the spinal nerve, there is a bifurcation into a dorsal and ventral ramus. The dorsal rami of spinal nerves innervate skeletal muscles of the back, while the ventral ramus innervates skeletal muscles of the trunk and limbs (Fig. 2.42).

The brachial plexus proceeds out of the neck into the upper limb and is organized around the axillary artery. The ventral rami of spinal nerves C5–T1 form the ***roots*** of the brachial plexus. These roots further organize into **trunks** then into **divisions** and **cords** of the brachial plexus before ending in terminal branches, which are the individual peripheral nerves innervating the upper limb (Fig. 2.45).

The individual roots merge into three trunks: the upper trunk (C5–C6), middle trunk (C7), and lower trunk (C8–T1). Each of the trunks splits into an anterior and posterior division for a total of six divisions. These six divisions will regroup into three cords named according to their position relative to the axillary artery.

The posterior cord (lying posterior to the axillary artery) is comprised of the three posterior divisions and contains roots C5–T1. The lateral cord contains the anterior divisions of the upper and middle trunks and contains roots C5–C7. The medial cord is a continuation of the anterior division of the lower trunk and contains roots C8–T1.

There are many terminal branches to the brachial plexus, and in time you may need to familiarize yourself with all of them. For most IOM clinicians, however, being familiar with five is sufficient. The five terminal branches that provide motor innervation to the muscles of the upper limb are the following nerves: median, ulnar, radial, axillary, and musculocutaneous. Table 2.3 contains information on the nerves of the brachial plexus.

Table 2.3 Nerves of the brachial plexus

Nerves	Segment	Muscles	Motion	Sensation
Long thoracic	C5, 6, 7	Serratus anterior	Winged scapula	–
Supraclavicular	C5, 6	Supraspinatus	Shoulder abduction	–
Axillary	C5, 6	Deltoid	Arm abduction	Lateral arm below shoulder
Musculocutaneous	C5, 6, 7	Biceps and brachialis	Elbow flexion	Lateral forearm
Redial	C5–T1	Extensor carpi, radialis longus and brevis	Extension of elbow and wrist	– Posterior, lateral arm – Dorsum of hand
Median	C5–T1	– Pronator teres and quadratus – Flexor carpi radialis – Flexors of fingers	Flexion of wrist and fingers	– Radial palm – Palmer surface – Tips of lateral 3½ fingers
Ulnar	C8–T1	– Interossei and lumbricals – Adductor pollicis	Movement of medial 2 fingers	– Ulnar and dorsal palm – Medial 1½ fingers

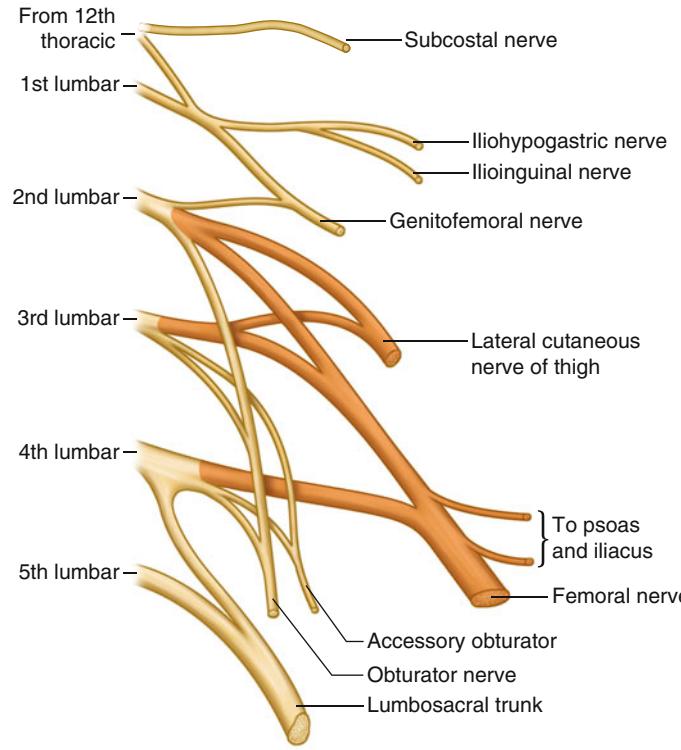

Fig. 2.46 Lumbar plexus

Lumbosacral Plexus

The anterior rami of the lumbar and sacral spinal nerves form a plexus that gives rise to the nerves of the lumbosacral plexus innervating the lower extremity and pelvis. It is convenient, however, to consider the lumbar and sacral plexuses separately.

The Lumbar Plexus

The **lumbar plexus** receives contribution from the ventral rami of spinal nerves L1–L4 with input from the subcostal nerve (T12) as well. The **lumbosacral trunk**, containing part of the L4 nerve and all of the L5, connects the lumbar and sacral plexuses (Fig. 2.46).

Table 2.4 Branches of the lumbar plexus

Nerve	Segment	Muscle	Motion	Sensation
Iliohypogastric	T12–L1	– Internal oblique – External oblique – Transversus abdominis	Anterior abdominal wall	– Inferior abdominal wall – Upper lateral quadrant of buttock
Ilioinguinal	L1	Internal oblique	Anterior abdominal wall	– Inferior medical inguinal ligament – Genitalia
Genitofemoral	L1–L2	Cremaster	Testicular	– Inferior medical inguinal ligament – Spermatic cord
Lateral femoral cutaneous	L2–L3			– Anterior, lateral and posterior aspect of thigh
Femoral nerve				
1. Anterior division	L2–L4	– Sartorius – Pectineus	– Medical aspect of lower thigh – Adduction of thigh	– Anterior medical skin of thigh
2. Posterior division		Quadriceps	– Knee extension – Patellar movement	– Anterior thigh hip and knee
Obturator nerve				
1. Anterior division	L2–L4	– Gracilus – Adductor longus – Adductor brevis – Pectineus	Thigh adduction	– Posterior medical thigh – Medical knee – Hip
2. Posterior division		– Adductor magnus – Obturator externus	Thigh adduction with lateral hip rotation	– Knee

The nerves of the lumbar plexus provide sensory and motor innervation primarily to the anterior compartment of the thigh. Two of these nerves (genitofemoral and lateral cutaneous femoral nerve) pierce the psoas muscle and are at greater risk during lateral approach minimally invasive spine surgery. Table 2.4 contains detailed information on the nerves of the lumbar plexus.

The Sacral Plexus and Sciatic Nerve

The sacral plexus provides sensory and motor innervation to the posterior thigh, leg, foot, and pelvic area (Fig. 2.47). The sacral plexus is formed by the lumbosacral trunk as well as anterior divisions of S1–S3. The largest nerve of the sacral plexus is the sciatic nerve, having contributions from L4–S3. The sciatic branches to form the tibial nerve and the common fibular nerve also called the peroneal nerve. Table 2.5 contains detailed information on the nerves of the sacral plexus.

Pudendal Nerve

The pudendal nerve receives contribution from S2–S4 and innervates the genitalia as well as the sphincter muscles of the bladder, rectum, and anus. Pudendal nerve EMG monitoring using electrodes placed in the external anal sphincter is indicated when the lower sacral spinal cord segments are at risk (as is the case during surgery near the level of the conus medullaris) or when there is significant risk posed to the cauda equina such as during a spinal cord untethering.

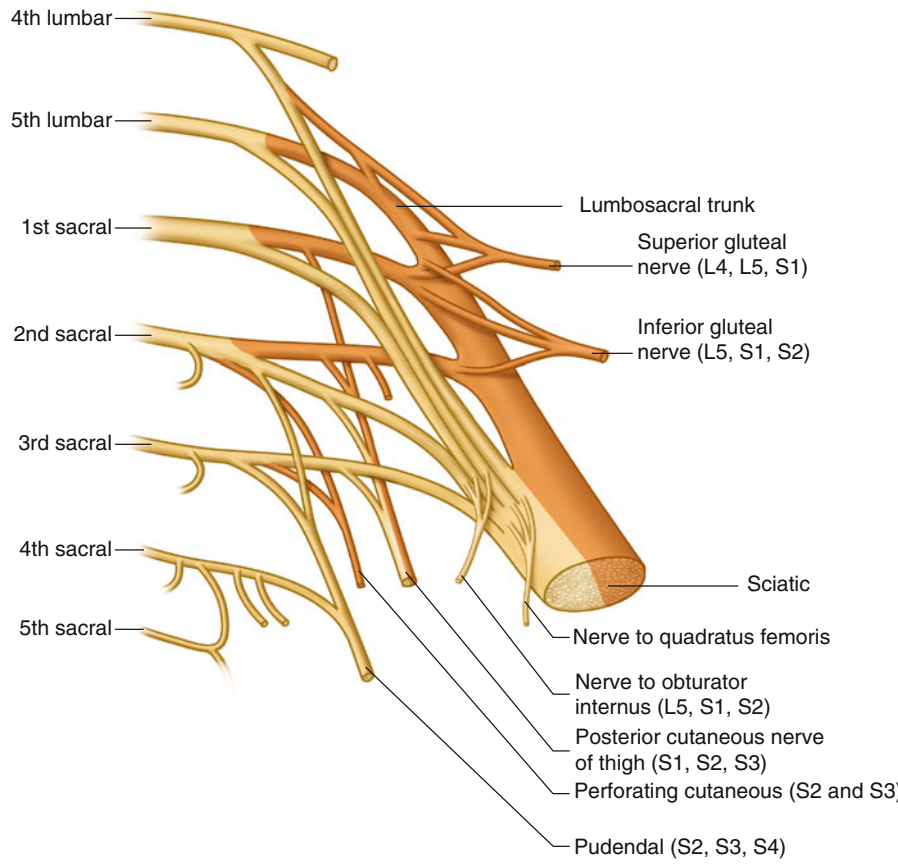

Fig. 2.47 Sacral plexus

Table 2.5 Nerves of the sacral plexus

Nerves	Segment	Muscles	Motion	Sensation
Sciatic nerve				
1. Tibial	L4–L5	– Biceps femoris – Semitendinosus – Adductor magnus – Popliteus – Gastrocnemius – Soleus – Flexors of foot	– Knee extension – Plantar flexion – Toe flexion	– Heel – Sole of foot – Hip – Knee – Ankle
2. Peroneal	L4–S3	– Biceps femoris – Peroneus longus – Peroneus brevis – Extensors of foot – Extensors of toes	– Knee flexion – Foot flexion	– Anterior leg – Dorsum of foot – Knee – Ankle
– Superficial				
– Deep		– Extensors of foot – Extensors of toes	– Dorsiflexion of foot and ankle	– Web space of first toe – Ankle
3. Sural	Components from peroneal and tibial			– Posterior calf – Lateral border of foot and fifth toe

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Cellular Neurophysiology

3

Scott Francis Davis

Introduction

The functional cell type of the nervous system is the neuron. Neurons are cells whose function is to process and transmit information through specialized connections called synapses. Neurons are electrically excitable cells, which means they are capable of transmitting an electric current known as an action potential. Neurons communicate with each other and with muscle cells by means of action potentials. This chapter will introduce you to basic neuronal morphology as well as the electrochemical basis of neurotransmission.

Neuronal Morphology

There are many types of neurons, but the many types can be boiled down to sensory neurons, motor neurons, or interneurons. Sensory neurons transduce external stimuli (such as touch, pain, temperature, light, sound) into action potentials that are moved throughout the nervous system to convey information. Motor neurons govern both voluntary and involuntary movement, generally in response to external stimuli. The role of interneurons is to relay information within the central nervous system.

A typical neuron has a cell body or soma that contains the nucleus and organelles. Two types of processes are found on a neuron. Dendrites are small processes emanating from the soma that receive incoming signals from other neurons. The axon proceeds from the cell body and functions to transmit impulses from the neuron onto other neurons or muscle cells. The axon hillock is the initial segment of the axon, rich in sodium channels, where the action potential is generated. The axon may branch along the way, and each branch ends as a specialized structure known as the terminal bouton. The terminal bouton lies adjacent to a postsynaptic element (the membrane of another neuron or muscle cell). Neuronal axons may contain an insulating material known as myelin at regular intervals along its length. Myelin is a lipid that is produced by support cells of the nervous system known as neuroglia. There are several types of neuroglia in addition to the ones that produce myelin. Schwann cells are the myelin-producing cells of the peripheral nervous system, and oligodendrocytes are the myelin-producing cells of the central nervous system. The spaces along the axon between myelinated segments are known as nodes of Ranvier. The purpose of this myelin sheath is to speed up conduction. Since myelin is an electrical insulator, action potentials won't cross myelinated segments of the axon and instead jump between nodes of Ranvier. This type of conduction is known as saltatory conduction. Figure 3.1 shows a typical neuron.

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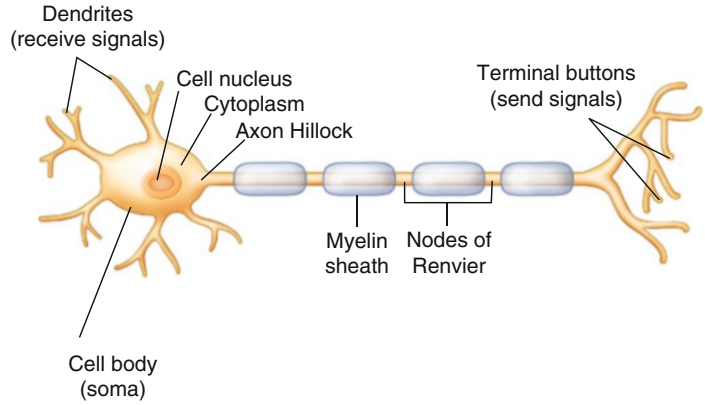

Fig. 3.1 The neuron

Neuronal Membrane

Like all mammalian cell membranes, the neuronal membrane is constructed of a phospholipid bilayer conferring upon the membrane the property of selective permeability (Fig. 3.2). Ions, charged atomic particles, are by nature hydrophilic and thus unable to freely cross the cell membrane. This sets up a gradient across the neuronal membrane resulting in a separation of ions according to concentration and electrical charge. This is called an electrochemical gradient. Separation of ions is synonymous with separation of charge and is the basis of the neuronal membrane potential. Neurons and muscle cells are able to move charge (ions) across the membrane and are thus termed electrically excitable cells. This movement of ions is accomplished through transmembrane proteins that serve as ion channels. We will discuss the role of ion channels in maintaining the resting membrane potential as well as generation of the action potential.

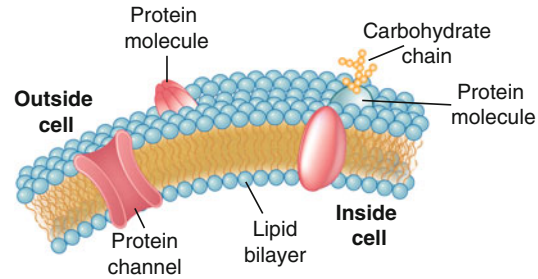

Fig. 3.2 Phospholipid bilayer. The neuronal cell membrane is composed of a phospholipid bilayer studded with transmembrane protein molecules. Among the varied functions of the transmembrane proteins is transporting ions across the cell membrane, an activity necessary for electrical excitability

Ion Channels

Ion channels are transmembrane proteins which provide a hydrophilic pore through which ions may pass between the cytoplasmic and extracellular sides of the membrane. Ion channels may be selective for either cations or anions or even for a specific ion. Ion channels are opened and closed in response to some event such as a change in membrane potential or the binding of a neurotransmitter.

Voltage-gated ion channels open and close in response to changes in the membrane potential and are termed voltage-gated ion channels. These ion channels are involved in propagation of the action potential. Each voltage-gated ion channel has a different activation range, defined as the range of voltages at which the channel remains open. The change in membrane potential that accompanies the opening of voltage-gated ion channels ironically results in their closure and opening of other voltage-gated channels. Such an interplay occurs between voltage-gated sodium and potassium channels during the propagation of the action potential.

Ion channels that are gated by the binding of a molecule (ligand) are termed ligand-gated ion channels. Neurotransmitter receptors are a type of ligand-gated ion channel. The binding of a neurotransmitter to its receptor is responsible for the initiation of the action potential or other postsynaptic signaling events. Signaling between neurons is accomplished through neurotransmitter receptors. When a neurotransmitter binds its receptor, it induces a conformational change (opening) in the receptor protein allowing the passage of ions across the membrane. The result is a change in membrane potential that can lead to an action potential. We'll discuss this in more detail below.

Excitatory neurotransmitters such as glutamate or acetylcholine bind to and open nonselective cation channels that allow Na+, K+, or Ca2+ to move across the membrane. Inhibitory neurotransmitters such as GABA and glycine bind to and open chloride channels.

Glutamate is the main excitatory neurotransmitter of the central nervous system. Acetylcholine (ACh), while found in the brain, is also the neurotransmitter of the neuromuscular junction. GABA is an inhibitory neurotransmitter found mainly in the brain, while glycine is the main inhibitory neurotransmitter of the spinal cord.

The Membrane Potential

The separation of ions across the membrane results in a recordable (nonzero) membrane voltage (Fig. 3.3). This resting membrane potential is approximately 60–70 mV in a typical neuron. By convention we indicate the polarity of the potential with respect to the charge on the inside of the cell. The intracellular space bears a negative charge with respect to the extracellular space; therefore, we say that the usual resting membrane potential of a neuron is approximately –70 mV.

The term "potential" in membrane potential indicates that there exists the drive for ions to move across the membrane. Remember that these ions are separated by the selectively permeable membrane and are unable to move freely. Ions want to move down their electrochemical gradient. If we were to allow ions to move freely across the membrane, the membrane potential would reach a value at which the ion was at equilibrium

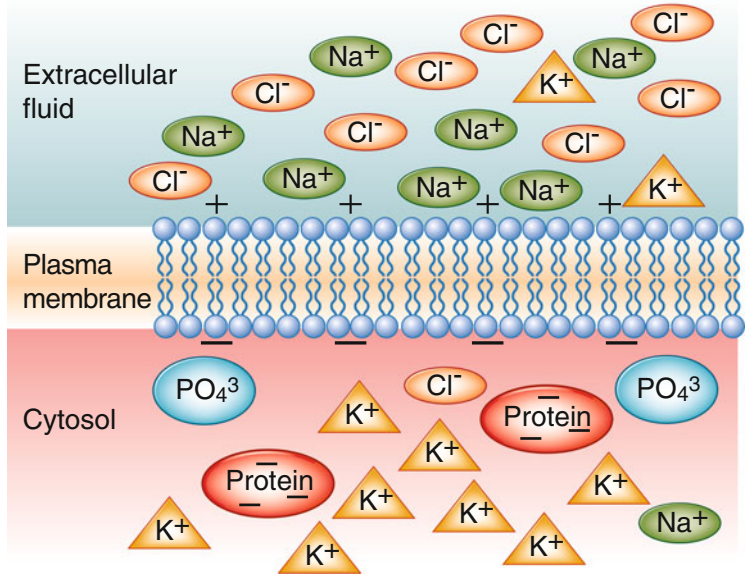

Fig. 3.3 Membrane potential. The separation of ions across the neuronal membrane is the basis of the membrane potential. Sodium is more abundant extracellularly and potassium is in greater concentration on the inside of the cell. Potassium leak channels and the sodium–potassium pump create a local negative charge along the intracellular membrane

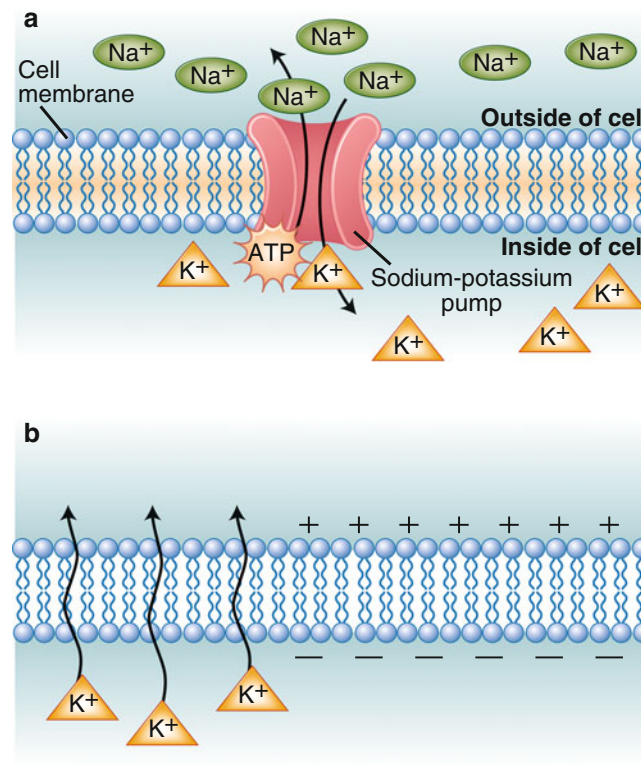

Fig. 3.4 (**a**) The sodium–potassium pump uses the energy derived from ATP to pump sodium and potassium against their concentration gradient. The pump moves 3-Na+ ions out for every 2-K+ ions into the cell causing a net negative charge to form on the intracellular membrane. (**b**) Potassium leak channels contribute to the negative resting membrane potential, and this leak must be balanced by the sodium–potassium pump so that the resting membrane potential doesn't run down leaving the cell unexcitable

and there would be no net movement across the membrane. In other words we would say the ion would be "happy." The membrane potential at which this would occur is called the equilibrium potential, and each ion has its own equilibrium potential. The potassium equilibrium potential is approximately −85 mV, while the sodium equilibrium potential is nearly +35 mV. Remember that the typical resting membrane potential is −70 mV. This means that potassium is much "happier" than sodium at rest; however, if allowed to move, it would still try and change the membrane potential to −85 mV.

The resting membrane potential is established and maintained by two mechanisms: potassium leakage out of the cell and the sodium–potassium pump (Fig. 3.4).

There are potassium channels, which allow passive movement of potassium out of the cell (along its concentration gradient). This movement of positive charge out of the cell makes the membrane potential more negative (it is trying to reach −85 mV). These channels are called potassium leak channels. The potassium leak channels are the reason that the resting membrane potential lies so close to the potassium equilibrium potential.

So if potassium is allowed to leak out of the cell, why doesn't the membrane potential reach the potassium equilibrium potential of −85 mV? The answer is the sodium–potassium pump. The sodium–potassium pump is a transmembrane protein; actually it is an enzyme that hydrolyzes a molecule called adenosine triphosphate (ATP). Think of ATP as the energy source of the cell. The reason that the sodium–potassium pump hydrolyzes ATP is because it needs energy input to perform its function. The role of this pump is to move three sodium ions from the intracellular to the extracellular space and two potassium ions from the extracellular to the intracellular space. This is *against* the concentration gradient of both of these neurons, hence the reason we needed energy input. The sodium–potassium pump is said to be electrogenic because it moves three positive charges out of the cell for every two positive charges into the cell. This creates a net charge of −1 inside the cell.

The Synapse

Signaling between neurons is through electrochemical transmission across the synapse. The synapse is the point of communication between neurons or between a neuron and muscle (Fig. 3.5). The synapse consists of a presynaptic membrane (the terminal bouton) and a postsynaptic membrane (a dendrite or muscle end plate). A small space, the synaptic cleft, separates the pre- and postsynaptic membranes. When an action potential is propagated down the axon of the presynaptic neuron, it invades the terminal bouton and opens voltage-gated calcium channels allowing calcium into the terminal. This sets up a chain of events resulting in the release of neurotransmitter into the synaptic cleft. Neurotransmitter in the cleft binds to its specific receptor on the postsynaptic membrane allowing ions to move across the membrane. If the neurotransmitter is excitatory (e.g., glutamate), sodium and potassium move into the postsynaptic neuron. If an inhibitory neurotransmitter is release, chloride is the ion that moves.

Postsynaptic Potentials

The movement of ions across the postsynaptic membrane in response to neurotransmitter binding creates a measurable change in the membrane potential of the postsynaptic cell. Excitatory signals cause a depolarization of the cell, while inhibitory signals result in hyperpolarization (the membrane potential becomes more negative). At any moment, a neuron is receiving multiple synaptic inputs (up to millions), some of them excitatory and some inhibitory. Each input generates a change in the membrane potential called a postsynaptic potential (PSP). A PSP may be excitatory (EPSP) or inhibitory (IPSP). EPSPs depolarize the neuron, while IPSPs hyperpolarize the neuron. PSPs decay with distance traveled across the membrane (Fig. 3.6).

Summation

PSPs summate and the effect on the membrane potential is equal to the summated PSPs. For example, if an equal number of EPSPs and

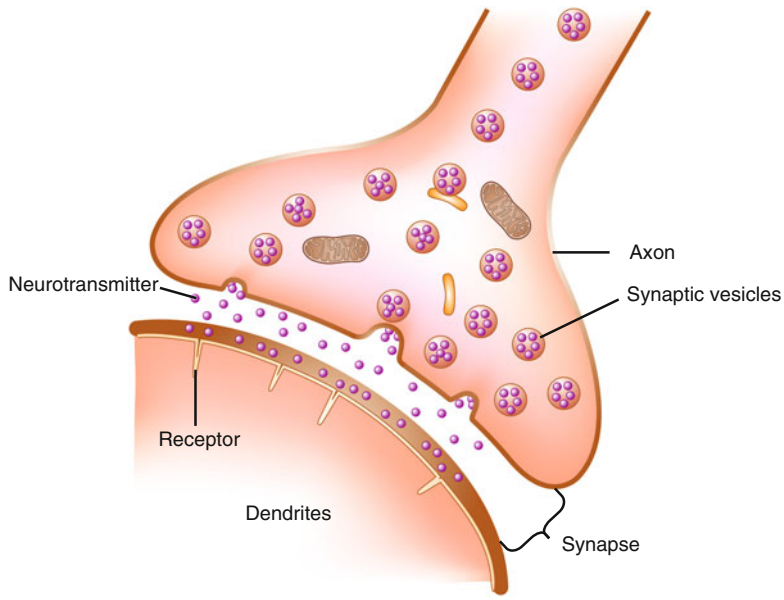

Fig. 3.5 The synapse

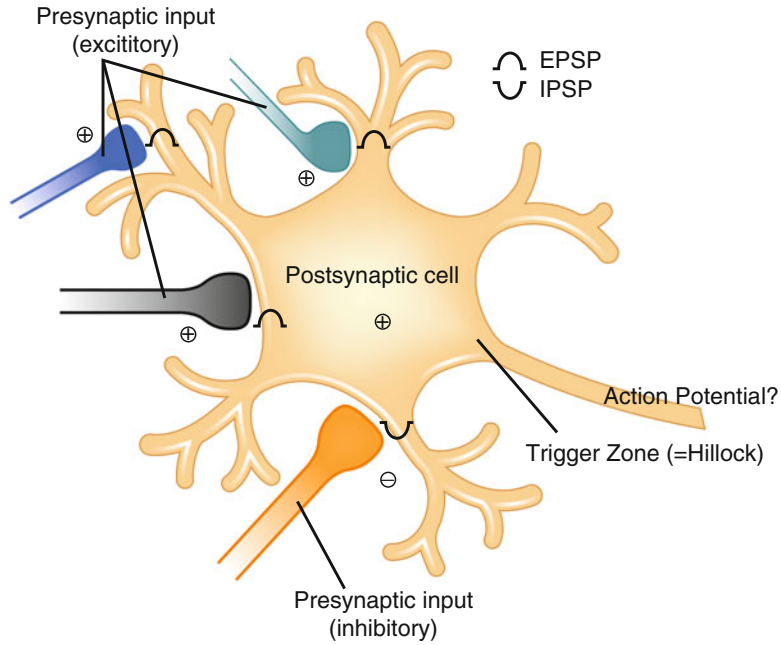

Fig. 3.6 Postsynaptic potentials. An example of a neuron receiving both EPSPs and IPSPs that will summate to possibly generate an action potential

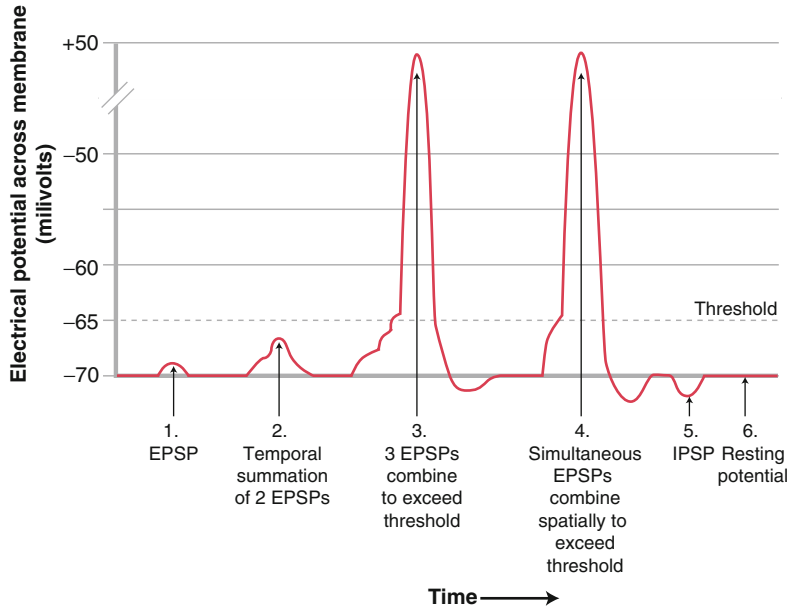

Fig. 3.7 Summation of postsynaptic potentials

IPSPs of equal magnitude reach the postsynaptic membrane at the exact same time, they cancel each other out, and there is no change in postsynaptic membrane potential. A greater number or magnitude of EPSPs depolarizes the cell, while a greater effect of IPSPs will hyperpolarize the membrane. Summation of PSPs can be either temporal or spatial (Fig. 3.7). Temporal

summation occurs from the overlap of PSPS that occurs when synaptic input is occurring at a high frequency. Spatial summation occurs in response to multiple convergent inputs to the cell at the same time.

Action Potentials

Action potentials are the short lasting electrical events that drive communication between neurons and between neurons and muscle cells. Action potentials occurring in muscle cells are the first step in a chain of events leading to muscle contraction. Unlike PSPs, action potentials are "all or none," meaning they do not vary in amplitude. They also self-propagate all the way down the axon as opposed to PSPs which decay with distance. In order for a neuron to fire an action potential, the neuronal membrane must depolarize to a specific voltage called threshold. The membrane may reach threshold in response to the summation of EPSPs received as the signals of presynaptic neurons. A predominance of IPSPs will bring the membrane potential further from threshold and prevent the cell from firing an action potential.

When EPSPs summate allowing the neuron to reach threshold, voltage-gated sodium channels open allowing sodium into the cell and causing a further depolarization. The influx of sodium will cause the membrane potential to move toward the sodium equilibrium potential (around +35). Before the membrane can reach the sodium equilibrium potential, the voltage-gated sodium channels will close (as the membrane potential moves outside of their activation range) and voltage-gated potassium channels will open ushering potassium into the cell and returning the membrane potential to rest (Fig. 3.8).

The depolarization of the membrane during an action potential is so strong that adjacent segments of membrane become similarly depolarized causing the action potential to propagate down the axon. This self-propagation ensures that action potentials travel the entire length of the axon without decrement.

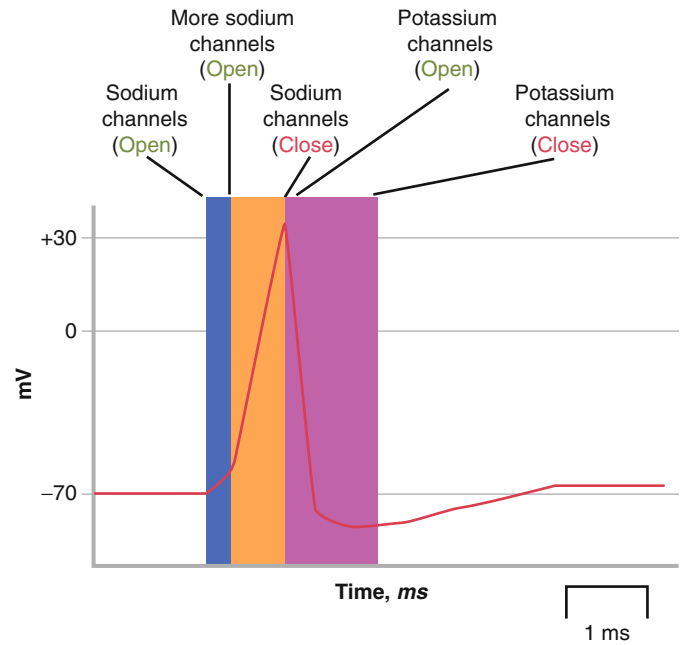

Fig. 3.8 The action potential. The interplay between voltage-gated sodium and potassium channels contributes to action potential generation

Neuromuscular Junction and the Motor Unit

The synapse between a neuron and muscle fiber is a specialized structure known as the neuromuscular junction. The presynaptic neuronal membrane lies adjacent to the end plate which is a specialized area of the sarcolemma, or muscle cell membrane.

Acetylcholine (ACh) is the neurotransmitter released by the neuron into the synaptic cleft, and ACh will bind its receptors on the muscle end plate. ACh receptors are nonselective cation channels that depolarize the muscle. This depolarization is the first step in a chain of calcium-dependent events leading to contraction of the muscle fiber.

Muscle fibers may receive input from only one axon terminal; however, each axon terminal may contact one or multiple (thousands) of muscle fibers. The axon terminal and all of the muscle fibers it innervates are called the motor unit (Fig. 3.9). Motor units may be small with axon terminals synapsing with very few muscle fibers or they may be large with each axon innervating thousands of muscle fibers. Muscles that require fine motor control are part of smaller motor units, while power muscles (such as those in the legs) are part of larger motor units.

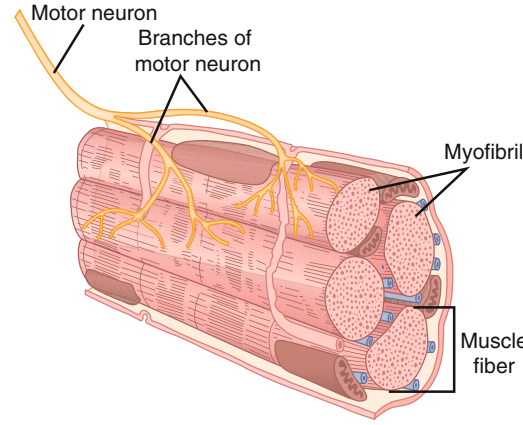

Fig. 3.9 The motor unit

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Electrophysiology and Bioinstrumentation

4

Jeremy Andrew Bamford and Scott Francis Davis

Introduction

Fundamental to intraoperative monitoring are the principles of electrical recording and stimulation of neural tissue. The monitoring clinician in the surgical suite will record neural activity that is both spontaneous and evoked by electrical stimulation in order to monitor and map the nervous system and ensure intact neural pathways. A conceptual understanding of these processes is one of the main pillars upon which the field of intraoperative monitoring is based. In the early history of intraoperative monitoring, neurophysiologists conceived of and built their own systems for electrically interfacing with the patient's nervous system. Today the equipment is purchased from companies that manufacture advanced monitoring devices that automate many of the calculations that had to be performed manually in the past. Nevertheless, the monitoring clinician in the surgical suite must have a working understanding of bioinstrumentation and electrical stimulation and recording techniques in order to ensure valid testing of neural function.

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Ohm's Law: The Basis of Bioelectrical Stimulation and Recording

There is a predictable relationship between current, resistance, and voltage. The flow of current across a resistive medium such as biological tissue generates a potential (also known as voltage or electromotive force). This relationship can be expressed mathematically as $V = IR$. This relationship is known as Ohm's law. We can see that the potential (or voltage, V) generated is the product of the current applied (I) and the resistance (R) of the circuit to that current. Current is measured in amperes (A). It is worth noting that current is not a measure of total charge delivered but actually the rate at which charge is delivered. The movement of charge is expressed in coulombs (unit of charge) per second. We can say that 1A = 1c/s. Although stimulus intensity is often given in milliamperes, the more clinically relevant issue is often the total charge delivered over a given procedure or even the total charge per stimulation phase (i.e., mono- or biphasic stimulation).

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DOI 10.1007/978-1-4614-8942-9_4,

Stimulation

Both nervous and muscular tissues are electrically excitable (sometimes referred to as irritable), meaning that they can be excited to activation with the application of an electrical current across their membranes. Electrical excitability is derived from the presence of voltage-gated ion channels embedded in the membrane (see Chap. 3 for a review of ion channels). Applying an electrical field across these tissues causes a depolarizing voltage potential across the membrane. If this depolarization is sufficient, the threshold for activation of the voltage-gated channels will be reached causing them to open and allow ions to flow along their gradients and generate an action potential. This action potential is primarily a function of sodium ions flowing into the cell from the extracellular space. If generated along an axon, the resulting action potential will propagate in both directions away from the original site of depolarization. From this point on, this electrically generated action potential is indistinguishable from physiologically generated signals. Electrical stimulation of nervous tissue may be used to monitor the functional integrity of the nervous system during surgery. For the purposes of intraoperative monitoring (IOM), we generally use gross stimulation of peripheral nerves, nerve roots, and the cerebral cortex rather than discrete stimulation of individual neurons. The result of this method of stimulation is recruitment of many (thousands or more) individual axons or cortical neurons.

Stimulating Electrodes

Stimulating electrodes have two poles: cathode and anode. The cathode is the stimulating pole and is the source of the current. The anode is called the return or current sink. Current will flow from the source generator to the cathode and return to the source generator via the anode.

To achieve controlled stimulation and pass an electrical current across the tissue, a cathode and anode must be in place. The stimulating electrodes can be arranged in a monopolar or bipolar configuration. In the monopolar variant, the cathode and anode electrodes are placed at some distance from one another. Usually, the cathode is placed nearer the tissue to be stimulated while the anode is placed at a distant site, often near a bony prominence or other location away from excitable tissues. This configuration generates a more diffuse electrical field that is appropriate for some stimulation tasks such as checking implanted screws for a pedicle wall breach or searching for a nerve within the surgical field. When it is desirable to achieve a higher degree of specificity when stimulating, such as for cranial nerve or cortical stimulation, a bipolar electrode configuration is used. A bipolar configuration involves placing cathode and anode closer together, often directly apposed across a specific nerve. Bipolar configurations limit the spread of current, generate greater selectivity of the excited neural tissues, and typically produce lower nerve activation thresholds. Common bipolar stimulation tasks include somatosensory evoked potentials where a distal nerve is activated to evoke a cortically measured response. In these tasks the cathode must be placed in a proximal position relative to the anode to avoid a condition known as anodal blocking. Anodal blocking occurs when a positive charge builds up under the anode. The nerve underlying this area of positive charge may become hyperpolarized leading to the abolition of an action potential attempting to travel through this region. For this reason the cathode is always placed proximal to the anode when attempting to electrically excite a nerve (for SSEPs) with a bipolar configuration.

Commercially available handheld monopolar and bipolar probes are available for a wide range of uses. Direct stimulation of peripheral nerves for the purposes of recording a nerve action potential close to the stimulation site actually is best achieved with a tripolar stimulator. Tripolar stimulators have a cathode flanked on either side by anodes. This reduces the recorded stimulation artifact and provides a very discrete stimulation site.

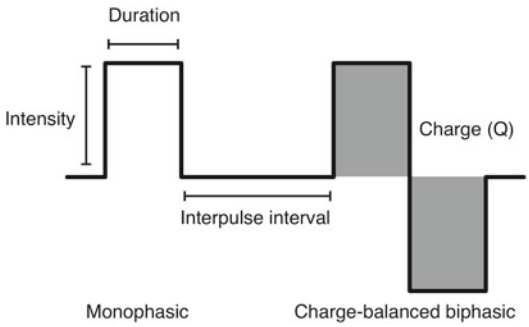

Fig. 4.1 Electrical stimulation is accomplished with simple square pulses, either monophasic or biphasic in nature. The pulses are described by their intensity (current) and pulse duration (time). The total charge is the product of the current and time. Symmetrical, biphasic pulses can be described as charge-balanced indicating that no net charge is delivered to the target tissue. The frequency of stimulation in Hz is the inverse of the interpulse interval

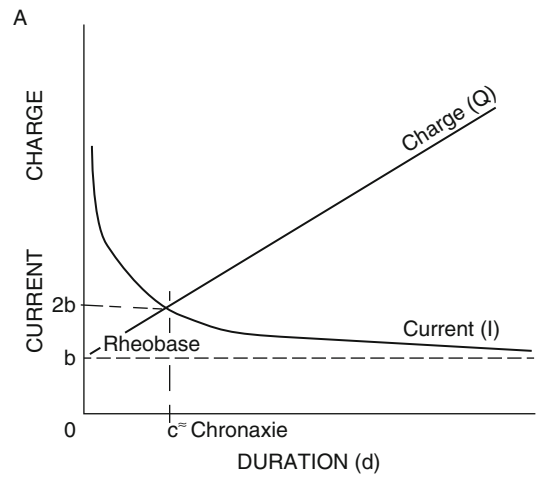

Fig. 4.2 Rheobase is the minimum stimulus amplitude needed to excite the target tissue, given an infinitely long pulse duration. Chronaxie is the pulse duration that excites neural tissue at twice the stimulus intensity of rheobase. This point also represents the lowest charge (Q, the product of stimulus intensity and pulse duration) at which the tissue can be excited

Stimulus Pulse

When stimulating electrically excitable tissues, we commonly make use of square-wave pulses of monophasic or biphasic configuration (Fig. 4.1). Square-wave pulses are rapidly rising pulses with simple morphologies that can be described by their pulse duration (or width) and pulse amplitude, usually referred to as stimulus intensity. Monophasic square pulses are of simpler configuration and are suitable for most stimulation tasks in the periphery where the cumulative length of stimulation is likely to be short. An example of this would be pedicle screw testing where the cumulative length of stimulation during a procedure can be measured in seconds. Biphasic pulses are more complex but have the advantage of being charge-balanced. This results in no net charge being deposited at the electrode–tissue interface. For stimulation tasks requiring prolonged stimulation times, a biphasic pulse should be selected in order to avoid corrosion of the electrode and deposition of potentially toxic substrates at the electrode–tissue interface. Chronically implantable stimulators such as deep-brain stimulators or epidural stimulators commonly employ biphasic, charge-balanced stimulation. Electrodes used for these stimulation tasks are frequently made from noble metals such as platinum or iridium rather than stainless steel. The combination of these is necessary to avoid corrosion or pitting of the electrode in a system that is designed to remain chronically active over years of use. Most stimulation tasks performed during a typical procedure will employ monophasic pulses. The most common exception is repetitive high-frequency continuous stimulation for brain mapping as may be performed by a device such as the Ojemann stimulator.

Chronaxie and Rheobase

Rapidly rising, square-wave pulses of either mono- or biphasic configuration can be described by their pulse duration and pulse amplitude. In order to understand the contributions of pulse duration and amplitude on the selectivity of neural stimulation, Lapicque undertook a series of investigations in the early 1900s using constant-current pulses. Lapicque described two concepts that illustrate the interaction between pulse duration and pulse amplitude and the excitability of neural tissues (Fig. 4.2). The first of these is rheobase which is the minimum stimulus amplitude needed to excite the target tissue, given an

infinitely long pulse duration (practically speaking >10 ms). Lapicque further discovered that doubling of the pulse amplitude from its rheobasic intensity greatly diminished the stimulus pulse duration necessary to excite a given tissue, thus reducing the total energy necessary to achieve excitation. The pulse duration at twice the rheobasic strength he coined as chronaxie. It has been shown that chronaxie may vary across neural tissues. While most white matter tracts have chronaxie values in the 50–100 μs range, gray matter structures can have chronaxie values above 200–700 μs. As a practical matter, while stimulating in the periphery, a pulse duration of 100–300 μs is often chosen as the selectivity of neural structures is less important for these tasks. One exception to this is the recruitment of H-reflexes where pulse duration of 1,000 μs is typically selected in an attempt to preferentially recruit sensory fibers (see Chap. 12 on H-reflexes). When directly stimulating the cortex, the pulse duration is typically kept shorter (50–100 μs) in an attempt to avoid exciting cell bodies, which may lead to ictal activity.

Constant Current vs Constant Voltage

Electrical stimulation can be applied in either a constant-current (current-regulated) or constant-voltage (voltage-regulated) manner. In the case of regulated voltage, the electromotive force (V) is held constant while the current (I) is allowed to fluctuate in response to changes in resistance (R), as dictated by Ohm's law. As a result of this method of stimulation, the charge and electrical field will fluctuate as current varies in response to changing resistance. Fluctuating resistance will result from changing conditions at the electrode–tissue interface; for example, if an electrode is slightly repositioned or the composition of the conductive medium that surrounds the electrode is altered. As the charge and electrical fields vary between stimulus trials, the elicited response may become unstable. Voltage-regulated stimulation is susceptible to unstable responses due to this alteration of charge and electrical field. In the case of current-regulated stimulation, the current is held constant while voltage is allowed to fluctuate in response to changing resistance. The primary advantage of this configuration is that the charge and electrical field generated are more consistent, resulting in a more stable response. This makes current-regulated stimulation preferred for environments prone to rapid and extreme changes in resistance such as an open craniotomy.

Concluding Thoughts on Stimulation

It is important for the monitoring clinician to be able to understand the variable methods of electrical stimulation in order to appropriately apply current in a safe and effective manner. An understanding of the concepts discussed will give the monitoring clinician the tools to be able to reason through a stimulation task and select the appropriate stimulus parameters. We can, however, sum up with some general recommendations for common stimulation tasks. Most of the stimulation tasks in the surgical suite will utilize bipolar stimulation (most evoked potentials, somatosensory evoked potentials, direct nerve stimulation), with the most obvious exception being pedicle screw stimulation. Likewise, most of the pulses will be monophasic in configuration, with the most obvious exception being direct cortical stimulation for brain mapping. Pulse duration will be in the range of 100–300 μs except for H-reflexes (1,000 μs) and cortical mapping (<100 μs). Most tasks will employ a constant-current stimulation (pedicle screw stimulation, direct nerve stimulation, somatosensory evoked potentials, direct cortical stimulation using the Ojemann system), while others will employ constant-voltage stimulation (motor evoked potentials). For more specific recommendations, the reader is referred to the chapters contained within this volume for each modality.

Recording

Recordings of electrical responses can be made from tissues that generate or transmit electrical signals. This process generates differences in electrical potential between anatomic structures,

which can be recorded by electrodes. Potential differences are generated by structures such as muscles, axons, and synapses that propagate electrical signals by the movement of ions across a membrane. Although a great many signals can be gleaned during an operation, those that relate to the integrity of underlying structures that might be injured during the procedure are identified for intraoperative monitoring. The presumption of intraoperative monitoring is that significant changes in the recorded signals represent potential injuries while preservation of baseline values should ensure that these structures and their associated functions are unaffected.

Recording Montages

Recording nomenclature can easily be confused with stimulation nomenclature. Most commonly, we make use of three montages or recording configurations. A referential recording is made whenever one electrode is placed over or near a generator of interest while a distant reference is placed in an electrically indifferent location such as over a bony prominence where little signal is expected. For instance, an electromyography (EMG) recording can be made from the medial gastrocnemius muscle with one electrode inserted over the belly of the muscle and a distant reference inserted over the medial malleolus. Such a configuration would have the advantage of sharing a large proportion of the ubiquitous electrical noise in common between the two channels, while not sharing much of the true signal of interest generated from the muscle. Referential montages are thought to give the largest signals; for this reason, they share little true signal in common between the two inputs, yielding little rejection of the true signal in the differential amplifier. A bipolar recording montage, not to be confused with bipolar stimulation, would be made if the distant electrode from the referential example above was moved from the medial malleolus to the medial gastrocnemius muscle. A bipolar recording is made when both recording electrodes are much closer together resulting in both electrodes recording some of the signal of interest. While less sensitive to activity generated at distances further from the electrodes, this configuration is highly specific. For this reason, bipolar recording is the most common montage employed in intraoperative EMG. The two adjacently placed inputs are ideally suited for recording the medial gastrocnemius muscle activity, although we can expect recordings of lower amplitude as some of their signals will be common to both inputs and thus be rejected by the differential amplifier. In practice, EMG signals are generally so large that a reduction of signal amplitude will be an acceptable trade-off when considered against the specificity advantage derived from the bipolar montage. Finally, we can also place needles in an active-referential montage by moving one of our needles to the lateral gastrocnemius muscle. By doing so we tie the medial and lateral gastrocnemius recordings together. The advantage of this configuration is that we can cover a larger number of muscles with fewer channels. When using modern intraoperative monitoring systems, this is often unnecessary as these newer machines have an ample number of channels (often 16–32) and there is no need to conserve channels for most procedures. The most likely exception would be a complex scoliosis procedure covering large areas of the spine and requiring monitoring from many muscles simultaneously. Should active-referential montages become necessary, the monitoring clinician must remember to combine muscles that arise from the same nerve root levels. For instance, creating a channel with one input over medial gastrocnemius, arising from the L5–S1 nerve roots, and another over tibialis anterior, arising from L4–L5 nerve roots, would be inappropriate as the monitoring clinician would be unable to accurately inform the surgical staff of the nerve root level at risk if EMG firing was noted from this channel. Similarly, a channel derived from the combination of biceps (C5–C6 nerve roots) and triceps (C6–C7) nerve roots would be inappropriate.

Volume Conduction

Volume conduction is the movement of charge through a conducting medium such as an ionic solution like salt water. This charge does not

propagate in a directed manner; rather it radiates in all directions. As such it follows the inverse-square law along with other radiant phenomena such as light and sound. The inverse-square law states that the intensity of the signal will decrease with the square of distance. This radiant behavior means that a recording of a volume-conducted signal will weaken with distance in any direction from the signal source. As currents move through the body, they interact with recording electrodes, producing a potential difference between the electrode pair and resulting in a signal that can be recorded and interpreted. For example, summated signals from neuronal populations generate the electrical potentials recorded from scalp electrodes, with individual neurons having their own contribution to that population signal. If the individual neurons are arranged randomly, these potentials will cancel each other out, yielding no recordable signal. This is described as a closed electrical field and can be observed in the configuration of many brain nuclei. Fortunately, many of the signal generators of interest to neurosurgical procedures are arranged in an ordered manner, yielding an open electrical field and signals that may sum together and can be recorded at a distance. For example, pyramidal neurons of the neocortex are arranged in layers and columns. These neurons fire synchronously, resulting in a large potential that is oriented across the recording electrode and thus recordable.

With most recordings made in the surgical suite, it is impractical to place the recording electrodes directly in contact with the signal generator. As such, recorded signals are almost always transmitted to the electrode via some degree of volume conduction.

Understanding Current Sources

Although the reality is more complex, sources of current in the body can be modeled reasonably well by imagining that the body is a homogenous container filled with a conductive saline solution. In this situation a single current source will radiate current spherically with intensity that declines with the square of distance. This is referred to as a monopole. Potentials around this perfect monopole will be equivalent at equivalent distance from the current source. Any potential measurement made at a given distance from the monopole will be equivalent so long as radius from the source is kept constant. We can envision shells of equivalent potential strength, known as isopotential or equipotential field lines surrounding the monopole. However, true monopoles rarely exist. More commonly, current flows between two oppositely charged locations creating a dipole. A dipole consists of two oppositely charged areas, one a source and one a sink, with current flowing between them. Many of the cortical generators measured in the surgical suite can be modeled as dipoles. Dipoles generate fields of opposing polarity across their midline. Relative to an indifferent reference, a potential measurement on one side of the midline will be equal in strength but reversed in polarity from one made on the other side. At the midline the fields generated by the opposing poles of the dipole will cancel out creating a plane of zero potential strength. This feature can be taken advantage of when mapping the cerebral cortex as the plane of reversal corresponds to the central sulcus (Fig. 4.3).

Near- and Far-Field Recordings

Recordings are often referred to as either near or far field. Although these terms describe distance relative to an electrical field generator, the concepts are only indirectly related to the distance between the recording electrode and the electrical generator of interest. There are significant underlying biophysical properties that distinguish how near- and far-field recordings must be made in electrically noisy environments like the surgical suite.

Near-field potentials are generally recorded by electrodes placed directly on the field generator or in close proximity. Although these recordings are made in close proximity to the generator, they are still compound recordings or the sum of multiple potentials. Near-field potentials tend to be specific to a discrete neural structure. Near-field recordings can be either

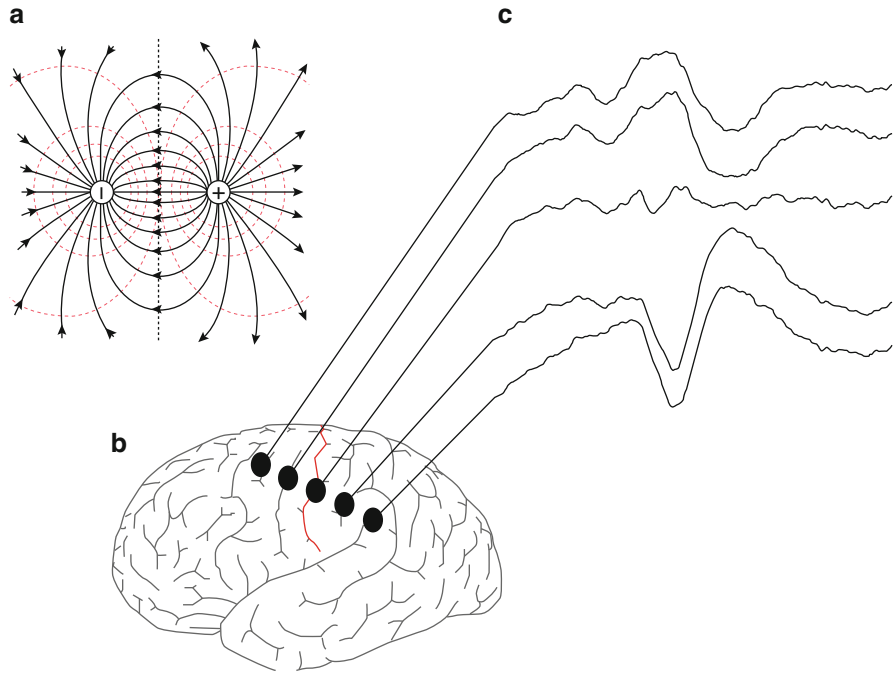

Fig. 4.3 An example of a perfect dipole (**a**), comprised of a current source and sink, and the field lines between them. The intersecting midline plane is an area of zero potential strength. Many neocortical generators can be modeled as current dipoles. An example is shown in (**b**) as the central sulcus divides the sensory areas (postcentral gyrus) from the motor strip (precentral gyrus). A grid of sensors can be laid across this strip, and evoked potentials can be recorded in response to sensory nerve stimulation (**c**). The reversal of phase from an upward deflection to a downward deflection in the recording represents the intersecting midline of zero potential generated from this structure. This can be used by the neurophysiological team to aid the surgeon in demarcating motor and sensory areas

bipolar (closely located reference) or referential (distant reference).

Far-field potentials are those recorded at a distance from the generator. As such, they tend to record the contributions of multiple structures and can be less easily identified with a specific structure. The amplitudes of far-field potentials tend to be lower than those of near-field potentials, and they usually require signal averaging of multiple sweeps in order to detect the signal from extraneous background noise. When recording far-field potentials, both electrodes are relatively distant from the generator source.

Noise

In any observation of a physical phenomenon, there is bound to be some error in the course of measurement. This is known as measurement error and is defined as the difference between the actual or true score and the observed score of a phenomenon. This is a real but intangible concept as the degree to which a measurement is contaminated with error can never be known perfectly. When making electrophysiological recordings, we often refer to measurement error simply as "noise." Ultimately, noise is any portion of the signal that may obscure the true signal. Sources of noise in the surgical suite can be varied, but one ubiquitous generator of noise emanates from electrical sources. In order to reduce the various noise components of our recorded signals, we employ methods including isolation of recording equipment from sources of noise, differential amplification, filtering, and signal averaging. The ultimate goal of all of these efforts is to maximize the signal-to-noise ratio (SNR).

Signal-to-Noise Ratio

SNR is the expression of the amplitude of the signal as a ratio with the amplitude of the unwanted noise. Mathematically, the peak-to-peak signal is divided by the largest peak-to-peak noise sample in the recording to calculate SNR. By convention, signals with SNR >2:1 are accepted and considered reliable. Signals with SNR <2:1 are deemed unreliable and should be treated as unmonitorable until SNR can be improved. Although the calculation of SNR is simple, the optimization of SNR involves a troubleshooting process that can be involved. The basis of the optimization of SNR is achieved with an understanding of the concepts of amplification and filtering that will be explained.

Amplification

Neurophysiological signals range in peak-to-peak amplitude <1 μV up to a few mV. In order to assess signals this small, it is necessary to increase the signal size, a process known as amplification. Ideally, amplification should increase the power of a signal without modifying its latency or morphology. The degree to which amplification increases signal power is called the gain. Gain can be expressed as the ratio of the amplitude of the output signal to the amplitude of the input signal (V_{out}/V_{in}). For instance, the gain might be set at 10:1 or 1,000:1 signifying that the output signal is more powerful than the input by a factor of 10 or 1000, respectively. As the factor rises to amplify very small signals, it becomes convenient to express such large numbers using a logarithmic transform, the decibel scale. Decibels are calculated as 20 times the base-10 logarithm of the gain ratio ($20\times \log10\ (V_{out}/V_{in})$. The decibel scale is convenient because it can express a large range using small numbers and because the gain of amplifiers in series can be added together to determine the final gain, rather than multiplying the untransformed factors together.

It should be noted that the term gain is improperly used in many intraoperative systems. True gain is an amplifier property, not a display sensitivity setting. In most systems both the gain (i.e., the ratio of signal amplification in the amplifier) and the display sensitivity (the setting that alters the way the signals are displayed onscreen) can be adjusted. But the monitoring clinician must always understand that these are not the same thing. Both the gain and the display sensitivity must be optimized if neurophysiological signals are to be properly interpreted.

Differential Amplification

The first stage of amplification is accomplished by a preamplifier. Preamplifiers are designed to produce low-noise amplification on the order of 10×–1,000× (20–60 dB). Preamplifiers are often placed close to the signal source to prevent contamination from sources of noise. Preamplification is necessary in order to increase the signal strength and maintain SNR before the signal is contaminated by any noise or interference. Once the signal strength is boosted by 20–60 dB, a later introduction of noise is much less likely to alter or abolish the signal.

In clinical settings, secondary amplification makes use of differential amplifiers that allow us to alter the gain of the amplification in order to optimize the output signal. In addition, differential amplifiers increase the components of the signal that differ between two inputs. These two inputs are referred to as the inverting and noninverting inputs, or sometimes as the active and referential inputs, respectively. Measurements are made from each input with reference to ground, the signal presented to the inverting pole of the differential amplifier is inverted, and the two inputs are added together (Fig. 4.4). The principle of differential amplification is that much of the signal that is common to both inputs is likely to be noise and should be eliminated in order to allow the true signal to be revealed. For instance, electrical noise at 60 Hz is a ubiquitous contaminant in the surgical suite and can be greatly reduced by this process as all inputs are likely to share a great deal of this noise in common. In contrast, true neurophysiological components of the signal are likely to vary as they are recorded by inputs placed at different locations.

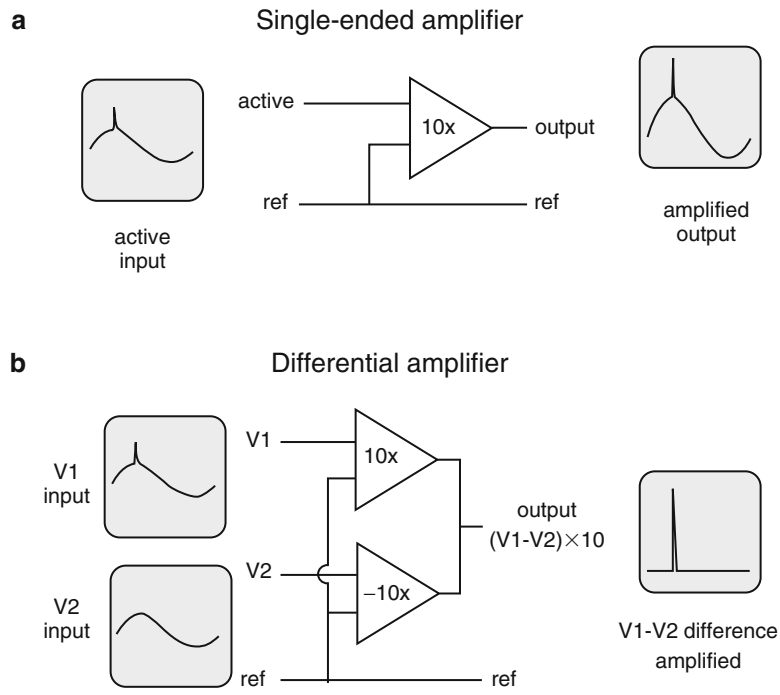

Fig. 4.4 In part (**a**) a single-ended amplifier is shown in which the input signal is simply increased in amplitude. No distinction is made between the active and referential inputs in this configuration. In (**b**) the differential amplifier compares the two channels, inverts one, and sums the final product together. Signals common to both inputs will be canceled, while differential signals will be amplified

Common Mode Rejection

The efficiency of rejection of common signals between the two inputs of the differential amplifier can be measured as the common mode rejection ratio (CMRR). The CMRR is often expressed using the same 20 log rule that is invoked for expressing the gain of an amplifier. The American Clinical Neurophysiological Society recommends that differential amplifiers used in the surgical suite have a CMRR of at least 80 dB or a 10,000:1 ratio of rejected to passed signals. In reality, modern equipment has a higher CMRR. It should be stressed that this process is dependent upon a low-impedance ground (<5 kΩ) and upon equal impedances between the two inputs (roughly equivalent to each other and also <5 kΩ) entering the differential amplifier. A high-impedance ground or significantly different impedances from the input electrodes often signify that the electrodes have been placed improperly and should be checked as this will result in a reduction of the CMRR and significant contamination of the true signal with noise.

Filters

Neurophysiological signals can be broken down into their component frequencies and visualized as a power spectrum with power on the ordinate (vertical axis) and frequency on the abscissa (horizontal axis) (Fig. 4.5). When this is done, we can see that neurophysiological signals collected in the surgical suite have frequency boundaries, beyond which no useful signal exists. Furthermore, there are frequencies that carry the bulk of the signal power and should be preserved if we are to accurately record a signal. The process of eliminating irrelevant frequency components and preserving critical ones is electronic filtering. A number of filter types exist,

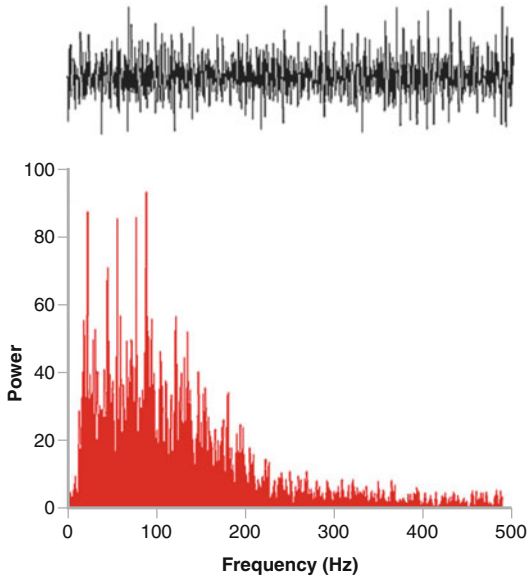

Fig. 4.5 An example of EMG firing is shown along the *top*. This signal can be deconstructed using statistical methods and displayed as a graph of the component signals of varying frequencies and their power. This example of surface EMG shows us that the majority of the signal power is contained at frequencies below 300 Hz. This knowledge is important when setting filters as it determines the optimal settings for low- and high-frequency filters

and their use can enhance or invalidate the recording process. Common filters include bandpass filters, notch filters, and artifact rejection filters. Furthermore, the filtering steps can be accomplished with analog or digital filters that produce a permanent or reversible modification of the incoming signal, respectively. Typically, all of these filters are employed in their proper place to aid in the recording of neurophysiological signals and optimize SNR (Fig. 4.6).

Bandpass

Extraneous signal energy that exists beyond the reasonable frequency range of a desired neurophysiological signal can be eliminated with bandpass filters. The bandpass is created by the use of low- and high-frequency filters (LFF and HFF). Some will refer to these as high-pass and low-pass filters, respectively, as they "pass" signals higher than, or lower than, the filter setting. Theoretically, signals with frequencies below or above these points will be completely eliminated from the recording. We can create a bandpass filter by setting our LFF at 30 Hz and our HFF at 1,000 Hz. This creates a bandwidth of 970 Hz, literally the range of the frequencies between the low and high filters. Published guidelines exist regarding the typical settings for bandpass filters for common modalities in the surgical suite.

Notch Filters

In contrast to bandpass filters, notch filters, also referred to as band-stop filters, pass most frequency components of a signal while eliminating those in a specific range. Notch filters are designed to eliminate noise at a very small range of frequencies. The most obvious example of a notch filter is a 60 Hz filter, or "mains" filter, designed to remove 60 Hz electrical noise from a recording. Notch filters are almost never applied to evoked potentials as they can cause ringing artifact in the averaged recordings. Although they can be applied to spontaneous recordings such as EMG, they are generally discouraged as the EMG signal contains a great deal of power around the 60 Hz frequency (Fig. 4.5). While 60 Hz noise can be attenuated, true signal in a critical portion of the power spectrum will also be lost. For this reason, it is preferable to remove 60 Hz noise through physical methods rather than applying a notch filter. These methods include unplugging sources of electrical noise, relocating the recording instruments away from such sources if they cannot be unplugged, and ensuring that cables from the recording instruments cross power cables from other devices at perpendicular angles.

Efficacy (Roll-Off)

Up to this point we have been discussing filters as if they have the ability to perfectly eliminate unwanted frequency bands from our physiological recordings. In practice this is not the case as filters do not completely eliminate unwanted signals but merely attenuate them in a graded manner (Fig. 4.6). The performance of this attenuation can be described by the cutoff frequency and roll-off.

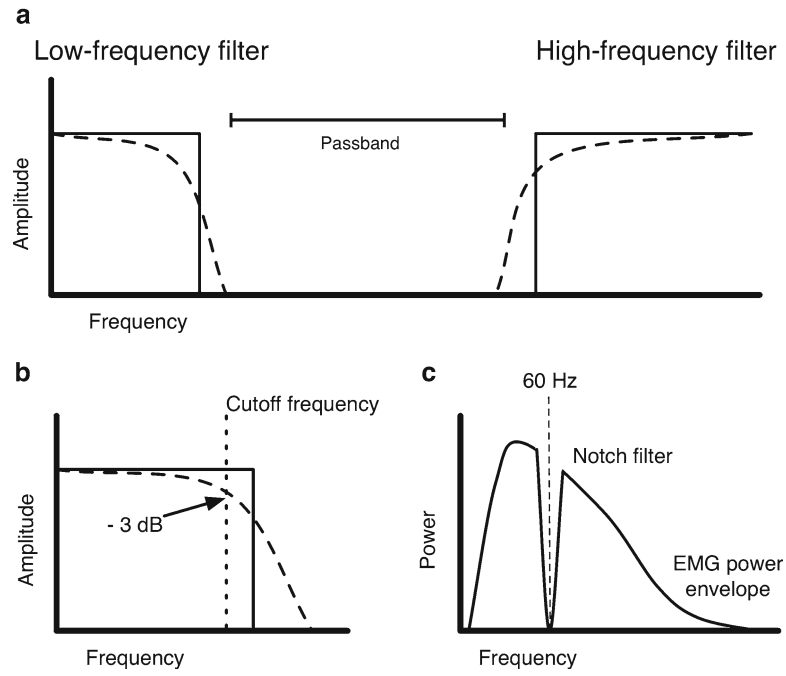

Fig. 4.6 Examples of common filter configurations are given. A passband is created in (**a**) in order to pass the desired frequencies while eliminating those above or below the selected range. The efficacy of filters is shown in (**b**) as the real filter performance (*dotted line*) deviates from the perfect orthogonal filter conception. Filter performance can be described by the cutoff frequency and the steepness of the slope. In (**c**) a notch, or mains, filter is shown against the envelope of signal power from a signal such as EMG. Although the notch filter can reduce unwanted 60 Hz noise, it can be seen that the filter eliminates all signal around the 60 Hz frequency. This represents a great deal of signal power from an EMG recording

The roll-off is the slope of the frequency attenuation curve. The cutoff frequency of a filter is the point at which 30 % or 3 dB of the energy of the signal has been removed. Roll-off describes how rapidly the power of the signal is attenuated beyond the filter cutoff. Steeper roll-offs are to be preferred as they indicate that the filter is acting in a more effective manner to attenuate signal beyond the filter stop frequency. Although we tend to imagine filter cutoffs as being absolute points beyond which no signal is passed, it is important to understand the limitations of filter effectiveness when setting filter boundaries.

Digital vs Analog Filtering

In clinical electrophysiology, we make use of both analog and digital filters. Analog filters are physical filters built into the circuitry, which permanently affect the signals being recorded. Analog filters are applied before digitization. The quality of analog filters depends upon the quality of their components and manufacturer, and they can suffer from imperfections arising from their physical construction. These include drift with changing time and temperature, nonlinearities in their function, and imperfect tolerances. In addition, analog filters can introduce a time distortion, especially in frequency components close to the filter cutoff. The introduction of a time distortion in certain components of the signal is referred to as a phase shift (Fig. 4.7). Low-frequency analog filters affect the slower frequency components of the signal (those closest to the low cutoff), causing them to appear earlier than faster components. This is known as phase lead. High-frequency analog filters affect the higher-frequency signal components (those closest to the high cutoff), causing them to appear later than slower components. This is known as phase lag. As a practical matter, phase shifts have little

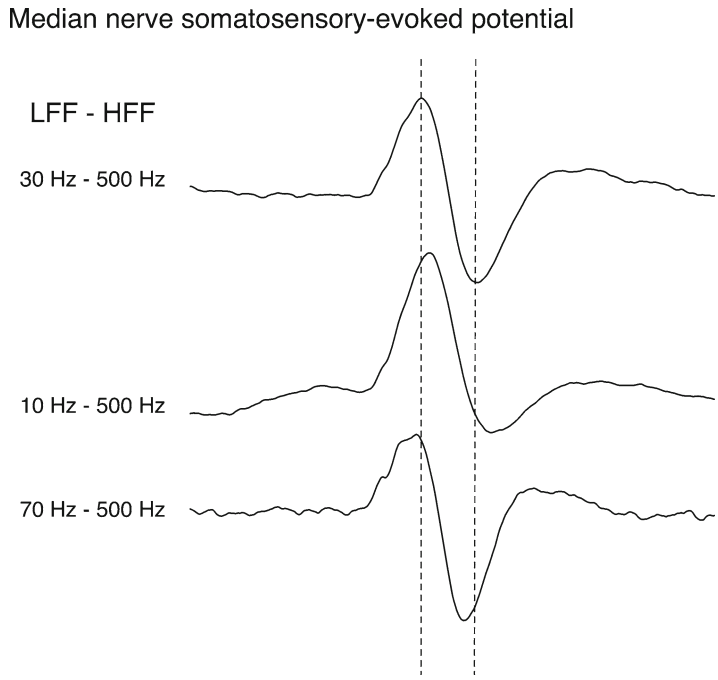

Fig. 4.7 A phase shift is demonstrated by altering the low-frequency filter settings for a median nerve somatosensory evoked potential. Adjusting the LFF to lower or higher settings causes a latency shift in subsequent recordings that could be misinterpreted as a cause for alarm

effect on the final signals so long as the filter settings are not adjusted during the course of a surgical procedure. The monitoring clinician in the surgical suite should understand that any changes in latency of evoked potentials following an adjustment of LFF or HFF are likely the result of phase shifts. From this realization it should be obvious that filters should preferably be set at the beginning of a procedure and not adjusted thereafter lest a real change in signal latency caused by a true surgical event be misinterpreted as the result of adjusting filter settings.

Digital filters have gained in popularity in signal processing as they do not suffer from these inconsistencies. Digital filters can be used to remove unwanted low and high frequencies with a very effective cutoff and without introducing phase shifts. However, they do introduce lag into the process as there is a tangible period of time required for the calculations involved in the digital filtering process. This lag has been reduced with increasingly powerful processors in the hardware systems used in for monitoring; however, these systems also introduce an added cost. In practice, digital filters are mostly applied in the surgical suite in the form of data smoothing operations.

Generally, analog filters are preferred for intraoperative monitoring as they are cost-effective and do not introduce a delay in signal processing. This is important as the interpretation of signals like EMG and EEG need to be communicated in real time to the surgical staff. Digital filtering is typically applied post hoc and in a reversible manner, as in the case of smoothing filters. It is generally preferable to avoid the use of smoothing filters in reading neurophysiological signals, as there is an inherent error introduced when digital filters are used. Nevertheless, reversible smoothing filters do not permanently degrade the signal data and may allow the monitoring clinician to capture monitorable data in very noisy environments. Circumstances exist where digital smoothing provides the only way to achieve monitorable signals.

Artifact Rejection

Artifact rejection filters are perhaps the simplest filters to conceive. They operate upon the principle that true neurophysiological signals are to be expected within a certain amplitude range.

Anything exceeding this range can be eliminated from the signal as being noise. Artifact rejection filters are an example of digital filters that are applied after the differential amplification stage. They are applied to evoked potentials that are time-locked to a stimulus volley. The most common use of artifact rejection filters is during the collection of averaged evoked potentials, and the most common source of rejected signals is the use of electrocautery. The signal recorded during electrocautery is often contaminated with high-amplitude artifact and unrecoverable by other filtering methods. Moreover, the artifact is of such high amplitude that if only a few sweeps, of the hundreds that may be averaged together, were to contain the electrocautery artifact, the final averaged signal would be unmonitorable. As such, rejection of these high-amplitude signals must be undertaken in order to be able to monitor during periods of electrocautery. If artifact rejection is not to be used, the monitoring clinician in the surgical suite will be forced to cease monitoring evoked potentials during the use of electrocautery.

Averaging

Many of the neurophysiological signals recorded in the surgical suite are measured in microvolts. Even after amplification and filtering, the noise and other background signals recorded alongside the true signal of interest are considerably larger. As such it cannot be expected that a single recorded sweep will yield a monitorable signal. The SNR of evoked potentials such as SSEPs can be improved greatly by a process known as averaging. Averaging works on the principle that the time-locked evoked potential present in each recording sweep will average together creating a larger amplitude signal, while random background activity in each recording sweep should cancel resulting in lower-amplitude background. The closer the background signals are to truly random signals, the more easily they will be averaged out. The improvement in the SNR resulting from signal averaging is quantifiable. The effectiveness of the averaging can be predicted by the formula $SNR_f = SNR_i * (\text{sqrt}(n))$, where SNR_f is the final SNR (after averaging), SNR_i is the initial SNR, and n is the number of sweeps. For example, if a single sweep has a SNR of 1:5, this can be improved to an SNR of 4:1 by averaging together 400 repeated sweeps ($1{:}5 \times \text{sqrt}(400) = 1{:}5 \times 20 = 4{:}1$). This improvement is most pronounced at lower numbers of sweeps. There is, in fact, diminishing return to increasing the number of sweeps. In the example above, the SNR is improved by a factor of 20 with 400 sweeps. A further doubling of the number of sweeps to 800 will take twice as long to produce a signal but increase the SNR by only an additional 40 %.

Stimulation Rates

For any evoked potential that is averaged, the opportunity exists to greatly attenuate the amount of noise that is averaged into the final signal by picking an optimal stimulation rate. In almost all cases, 60 Hz mains noise and various harmonics of this frequency will represent the greatest amount of steady-state noise experienced in the surgical suite and the greatest opportunity for improving SNR with optimal rates of stimulation. A harmonic is a frequency that is an integer multiple of the fundamental frequency. For instance the third, fifth, and seventh harmonics of 60 Hz noise will be 180 Hz, 300 Hz, and 420 Hz, respectively. These odd-ordered harmonics will almost always encompass the greatest amount of noise signal power. The noise encompassed in these frequencies can be averaged either in or out of the final averaged product. For obvious reasons we would prefer the latter. The first way to achieve this is to select a stimulus rate that is not a factor of the noise frequencies we experience in the surgical suite. A stimulus rate of 2 Hz, for instance, is a factor of 60 Hz and its odd-ordered harmonics. Selecting this stimulus rate will result in averaging a great deal of electrical noise into the final signal, most likely rendering it unmonitorable. On the other hand, a stimulus rate of 3.17 is not a factor of 60 or its odd-ordered harmonics and will result in a much better SNR of the final averaged signal. However, we can continue to

Table 4.1 The optimal stimulation frequencies for use while averaging out 60 Hz noise and its associated third, fifth, and seventh ordered harmonics

Stim frequency	60 Hz	180 Hz—third	300 Hz—fifth	420 Hz—seventh
2.00	30.00	90.00	150.00	210.00
2.18	27.52	82.57	137.61	192.66
3.17	18.93	56.78	94.64	132.49
4.44	13.51	40.54	67.57	94.59

The poorest options are factors of 60 such as 2 Hz stimulation that will actually average noise into the recording. The most optimal stimulation frequencies can be divided into 60 and its ordered harmonics and will be ½ period off of a real integer

improve our SNR if we select a stimulus rate that is an integer factor of the noise frequency + 1/2 period. To determine this, we simply divide the noise frequency by the stimulus rate. If we want to evaluate 3.17 as a stimulus frequency, for instance, 60/3.17 = 18.93. Although 3.17 is not a factor of 60, it is still suboptimal for our purposes as it is not equal to an integer factor + 1/2 period. On the other hand, if we evaluate 4.44, 60/4.44 = 13.51. The result is an integer factor of 60 + 0.51 (close to 1/2 period). A stimulus rate of 4.44 Hz then will average out a larger portion of the 60 Hz noise present in the recorded signal. We can create a simple chart that will predict the optimal stimulation rates to be used in the surgical suite in the presence of 60 Hz noise and the third, fifth, and seventh ordered harmonics thereof. As we can see from Table 4.1, the stimulus rates of 2.18, 2.79, and 4.44 Hz are best optimized to average 60 Hz and odd-ordered harmonic noise out of the signal. These stimulus rates should be the first choice when running averaged evoked potentials that require a relatively low stimulus rate, such as SSEPs.

Digitization

Thus far we have concerned ourselves with analog signals. Analog signals have the properties of being continuous and having an infinite number of points in the signal. Furthermore, an analog signal is a recorded signal that is directly proportional to the underlying physiological phenomenon. As such, the signal is analogous to the physiological phenomenon. Digital signals, on the other hand, are a sampled representation of the analog signal, created by quantizing the signal at discrete points in time. Digitization is necessary in order to import the signal into a computer for analysis. Humans tend to prefer to view data in analog form as waveforms or lines. As pattern-detecting creatures, we have an affinity for viewing changes in the data in this visual manner. Computers, on the other hand, are suited to mathematical analysis of the data and require a discrete set of numbers in order to apply mathematical operations and analyze the data.

Digitization is performed through the use of an analog-digital converter (ADC). It is important that digital representations of analog signals be as faithful to their analog templates as possible. The process of digitization involves both sampling and quantization. Put simply, sampling is the process of describing the signal as a set of discrete time periods, equal in length, over the whole signal. Quantization is the process of assigning a discrete amplitude value to the analog signal at each one of these time points. Digital signals must be accurately resolved or represented in both the horizontal (time) and vertical (amplitude) domains. Improper sampling or quantization will yield a final produce that has been corrupted and is invalid.

Sampling

Digital signals are resolved in the horizontal or time domain with a fidelity that is proportional to the sampling interval. The sampling interval is merely the time between each sample that is extracted from the analog signal. The inverse of sampling interval is the sampling frequency in Hz.

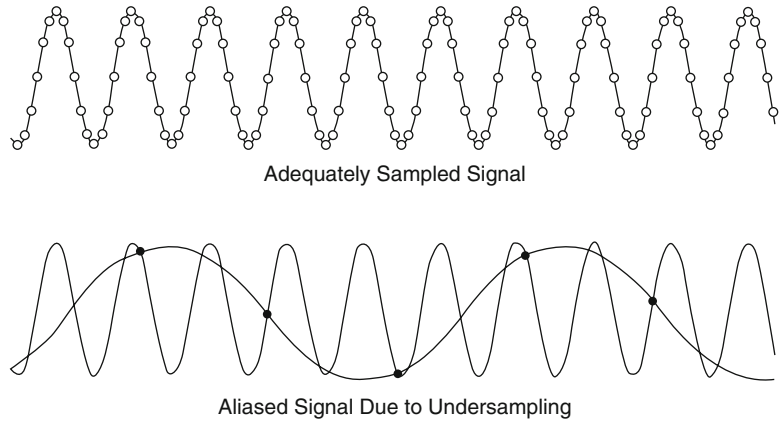

Fig. 4.8 The *top* figure was sampled at a high rate (*closed circles*), and the resulting waveform identically overlays the original. In the *bottom* example, the sampling rate was insufficient to create a high-fidelity digital signal. A curve connecting the samples creates a low-fidelity digital waveform

For instance, a sampling interval of 1 ms would yield a sampling rate of 1,000 Hz. This simply means that we are extracting a data point from the analog signal 1,000 times each second. Sampling and digitizing an analog waveform at a higher frequency results in a sampling of a greater number of points and a more accurate digital representation of the signal. However, it also requires greater computer power and memory capabilities. Sampling at too low a frequency will result in a failure to accurately resolve the signal on the horizontal axis. This process is known as aliasing.

Nyquist Theorem

So what frequency is appropriate for sampling a given signal? The Nyquist theorem states that in order to avoid aliasing, it is necessary to sample at a frequency that is twice the highest frequency component of the analog signal. While the Nyquist theorem represents the minimum sampling frequency to avoid aliasing, the optimum sampling frequency is three times the highest frequency component of the analog signal (Fig. 4.8). As we have mentioned, neurophysiological signals collected in the surgical suite have previously determined frequency boundaries, beyond which no useful signal exists. For instance, the majority of the signal power derived from a surface EMG recording is gathered at 300 Hz or less. By applying the Nyquist theorem, we can see that a minimum sampling rate to digitize this signal without aliasing would be 600 Hz, although 900 Hz would be optimal.

Quantization

Once the signal has been sampled, we must then undertake the process of quantization. This is the assignment of amplitude values derived from the analog signal at each time point. Note that this process involves some level of error as an analog signal with an unlimited set of values must now be represented by a digitized signal with a discrete set of values. The factor in this process that limits accuracy of the final signal is the number of bits available in the ADC. The number of discrete data points available is represented as 2^n, where n is the number of bits. For example, an ADC with 4 bits can be used to represent 16 unique values, while an ADC with 8 bits can be used to represent 256 unique values. Obviously, an ADC with a greater number of bits will allow a greater range and a greater resolution in our final digitized signal. The resolution that we apply will determine the accuracy limits of our newly digitized dataset. If the vertical

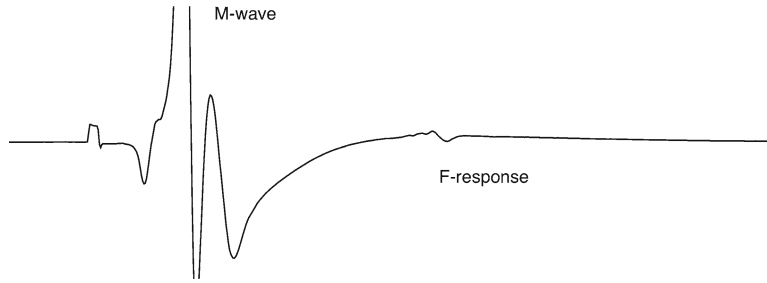

Fig. 4.9 A representative example of a recording made in the surgical suite is shown. The first portion, marked M-wave, has been clipped as some of its values fall above and below the range of the recording. The second part of the recording, marked F-response, is a very small amplitude response and is difficult to display with the range so broad. This is a visual representation of trade-offs that must be made in the quantization process. Having an ADC with a high bit count can help to alleviate this problem, as the dynamic range of the recording is increased so that high- and low-amplitude recordings can be resolved together

resolution is too limiting, our data will be clipped, as some of the values will fall outside of the range we have created. For instance, if we set a vertical range of ±10 μV, and the analog signal reaches 25 μV, this portion of the signal will be lost. On the other hand, if the vertical resolution is too large, our dataset will be lacking in accuracy as a small range of values will have to represent the entire amplitude of the analog signal. We will lose resolution as the small range of signals must be represented by a broad range of values.

Consider Fig. 4.9 and notice that the first part of the signal, the M-wave, has been clipped, while the second part of the signal, the F-response, is displayed with a rather small amplitude. This is the trade-off that occurs during quantization when selecting an input range or vertical resolution. If we optimize the range for the M-wave in this recording, the F-response will be too small to detect. On the other hand, if we optimize the range for the F-response, we will clip the M-wave, as has occurred in this example. In this case, a compromise was chosen so that the F-response could be viewed along with the M-wave; it was appropriate to clip the M-wave portion in order to view the F-response properly. This is a visual representation of what happens when the vertical resolution is suboptimal.

Concluding Thoughts on Recording

Recordings made in the surgical suite must accurately represent the true bioelectrical activity of the structures that are generating the signal. Advancing technology has given us the ability to make high-quality digital recordings in an electrically hostile environment with a minimum amount of difficulty. Although our current instrumentation eliminates the need for us to perform tedious calculations and continuously alter our stimulation and recording parameters, it is no less necessary for the modern physiologist to have a complete understanding of the concepts behind electrophysiological stimulation and recording.

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Anesthesiology and Intraoperative Electrophysiological Monitoring

5

Tod B. Sloan and Alan David Kaye

General Overview: Anesthesiology as the Practice of Perioperative Medicine

The role of the anesthesiologist during procedures where intraoperative electrophysiological monitoring (IOM) is being performed involves anesthetic titration, attaining physiological homeostasis, and medical management of the patient. Further, the anesthesiologist participates in mitigating neural injury when the monitoring indicates that the nervous system may be at risk for injury. More specifically, the choice of anesthetic agents directly impacts the ability to reliably record IOM responses, and the physiological management (e.g., blood pressure) impacts on the reserve of the nervous system to tolerate procedural trespass. When altered responses indicate the health of the nervous system may be compromised, the insights of the anesthesiologist and the ability to improve the physiological reserve are keys to reducing neurological risk. This chapter is written to discuss these aspects to improve integration of the anesthesiologist into the IOM monitoring team effort.

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Preoperative Planning

It should be noted that the role of the anesthesiologist extends throughout the peri-procedural period. Often referred to as the "internist in the operating room," anesthesiology is the practice of medicine which extends before and after the procedure. In the pre-procedural period, the anesthesiologist partners with the surgeon, the patient's usual healthcare provider, and if warranted, consultants to insure that the patient is in optimal shape in order to best tolerate the procedure with minimal overall health risk. The anesthesiologist evaluates those medical conditions that impact directly on intraoperative management to understand their pathophysiology and preoperative management so that this can be extended through the peri-procedural period. In particular, evaluations are very important regarding the management of cardiac-, pulmonary-, hepatic-, renal-, and pregnancy-related issues and specific medications taken by the patient. These conditions will also result in each patient being classified by the American Society of Anesthesiology (Table 5.1) and impact medication choice, which may force challenges and potential compromises with a typical anesthetic regimen for IOM.

Other pre-procedure considerations include assessment of the airway, positioning-related factors, intravenous access, pathophysiology of the

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Table 5.1 American Society of Anesthesiologists physical status classifications

1.	A normal healthy patient
2.	A patient with mild systemic disease
3.	A patient with severe systemic disease
4.	A patient with severe systemic disease that is a constant threat to life
5.	A moribund patient who is not expected to survive without the operation
6.	A declared brain-dead patient whose organs are being removed for donor purposes
If Emergency—add "E" (e.g., 2E)	

From: http://www.asahq.org/Home/For-Members/Clinical-Information/ASA-Physical-Status-Classification-System

surgical site, fluid management, and other issues which may impact on anesthesia medication choices for the procedure and management in the immediate recovery period (e.g., post-traumatic stress, trauma, elderly considerations, chronic alcoholism, or chronic opioid use). Airway issues, including anticipated difficult intubation or an unstable cervical spine, are extremely important and dictate an awake intubation or other alternative induction and advanced airway intubation methods. As such, the choice of muscle relaxants and sedative drugs may differ. As an example, the lack of intravenous access may necessitate an inhalational agent induction as is often used in children. Another example would be inducing anesthesia for a patient with increased intracranial pressure. In this case the blood pressure must be maintained high enough to preserve adequate cerebral perfusion pressure. Hence, in general (unless central venous pressure is extremely elevated), the net perfusion of the brain (cerebral perfusion pressure) is the mean arterial pressure minus the intracranial pressure (discussed along with other physiological relationships later in the chapter).

In the preoperative period, the anesthesiologist will usually discuss the planned procedure with the surgeon or proceduralist. Positioning, anticipated blood loss, special procedures (such as deliberate hypotension or hypothermia), and anticipated procedure risks are discussed to plan for anesthesia management and the preparation of ancillary equipment. This is also a time when the IOM team should confer with the surgeon to insure the optimal choice of monitoring modalities. Additionally, discussion between the entire team is warranted when surgical cases arise that require IOM team. The anesthesiologist, IOM team, and the surgeon should communicate before induction regarding optimal anesthetic choices in order to facilitate that monitoring. This communication is a standard of care to insure optimal patient outcome. In particular, the discussion between the IOM team and anesthesiologist should identify when the initial baselines need to be acquired, especially immediately post intubation or prepositioning, so that the induction can be planned with this consideration. It is important to recognize that the final choice of anesthetic medications may be a compromise between that which may appear optimal to the IOM team and that which may be dictated by medical and patient considerations identified preoperatively. Not infrequently, this discussion may result in a bargaining where the best compromise can be made. Once baselines are acquired, the anesthesia choice may be further adjusted based on how the patient is responding vis-à-vis hemodynamics and IOM.

Preoperative Discussion with the Anesthesiologist

The discussion with the anesthesiologist must take into consideration the experience and training of the specific practitioner, since they may need to consult with a colleague. The anesthetic is usually delivered and monitored by either a solo practitioner or by an "anesthesia care team." Solo practitioners include physician anesthesiologists or certified registered nurse anesthetists (CRNA). The care team model includes an in-room practitioner such as a CRNA, anesthesia resident physician trainee, student registered nurse anesthetist (SRNA), or an anesthesia assistant (AA) *with* anesthesiologist oversight. Physician anesthesiologists are individuals with a medical degree (MD or DO) who have completed a focused residency in anesthesiology and may have advanced training (fellowship) in subspecialty areas (e.g., neurosurgical, thoracic, cardiac, pediatric, or obstetric anesthesia). A CRNA is an advanced practice nurse with a master's degree who has undergone specific training in

anesthesia after nursing practice, typically in intensive care environments, and may work with a physician anesthesiologist or, in some circumstances, as a solo practitioner. Some CRNAs may have advanced degrees such as a doctorate in nursing practice (DNP). An AA has a master's level education with specific anesthesia training in classroom and practical course work. They can act as physician extenders who always work under the direction of physician anesthesiologists. Since their background, training, and experience will vary, each of these individuals may be more or less familiar with the anesthesia considerations for IOM, so preoperative discussion, especially the day before the procedure if possible, will be important for their planning.

Types of Anesthesia

Important for discussion with the anesthesiologist is to understand the terms used with regard to the delivery of anesthesia (in particular, the two ways the term "MAC" is used). First, although general anesthesia is usually used with IOM, anesthesia is also delivered in other ways. "Local MAC" is used to describe the use of intravenous medications (e.g., propofol and midazolam) in patients where local anesthesia is used (often by the surgeon or proceduralist) to anesthetize a limited region of the body. In this case, the term "MAC" stands for "monitored anesthesia care" and should not be confused with the similar term "MAC" used to describe the potency of inhalational anesthetics (see below). One of the goals of an anesthetic medication is sedation and usually amnesia. Blocking of noxious stimuli (such from the procedure) is primarily done by the use of local anesthesia. IOM is usually not utilized with monitored anesthesia care; however, electrocorticography and mapping of the motor and speech cortex is done by a specialized form of MAC when patients have "awake" craniotomies where local anesthesia is used on the scalp to allow a craniotomy (the exposed brain is insensitive).

"Regional" anesthesia is used to describe the delivery of anesthesia where only a part of the body is made completely insensitive to the surgical stimulation. For example, the patient may have local anesthesia injected to anesthetize specific nerves or plexus (such as a brachial plexus block anesthetizing an arm) or injected into the spinal or epidural space ("neuraxial" anesthesia). Similar to local MAC, sedation may be such that the patient becomes responsive to stimuli in a continuum from awake to unresponsive. Intravenous medications are used to produce sedation and usually amnesia. Blocking of noxious stimuli (such as from the procedure) is primarily done by the regional blockade. IOM is usually not possible with regional blockade of major neural structures as the local anesthetics used usually render the neural structures unable to conduct IOM signals. However, when regional anesthesia is conducted to anesthetize regions allowing access to structures for a procedure and the neural structures being monitored are not anesthetized, IOM can be used as long as the IOM technique is not painful. A good example is the use of electroencephalography during carotid endarterectomy where a cervical plexus regional blockade is often used to allow surgical access to the external carotid artery.

General anesthesia (GA) is the anesthesia usually used during most procedures where IOM is used. Typically, several medications are used together to produce a more comprehensive anesthetic, which involves four major anesthetic goals. First, medications are given to produce a state of unconsciousness where the patient does not respond to stimuli. Second, medications are delivered to insure that the patient has no awareness or recall (amnesia) during the procedure. Third, the anesthesia medications are used for analgesia and to block noxious stimuli from activating the nervous system. This goal is often termed antinociception and differs from local MAC and regional anesthesia where local or regional anesthesia is primarily responsible for this aspect. Preventing awareness and recall is a major concern of anesthesiologists and is a major concern in designing an intravenous anesthetic.

Fourth, medications are used in GA to block movement (e.g., muscle relaxation) of the patient in response to stimuli. Although this can be accomplished using medications which block transmission at the neuromuscular junction, the anesthetics

used for most cases where IOM is performed involve using agents to block the reflex transmission of sensory stimuli through the spinal cord producing peripheral motor activity. This reflex pathway involves afferent sensory input from the periphery, synaptic connections within the spinal gray matter, efferent motor pathways, and descending influences from the brainstem and cortex.

It is important to differentiate the reflex movement through the spinal cord pathways in the anesthetized, unconscious patient from the voluntary movement of an unanesthetized, awake patient. The comment "the patient is awake" when they move under anesthesia is usually incorrect since the motion is due to reflex activity in the inadequately anesthetized spinal cord from peripheral stimuli. This need for immobility is one of the major challenges and concerns for the anesthesiologist during procedures involving IOM when complete muscle relaxation must be avoided. The challenge for the anesthesiologist is that parts of the same pathway are used for reflex movement and for desired muscle activity from transcranial motor cortex stimulation (MEP). This suggests that the titration of effect in the efferent components (spinal gray matter and peripheral nerve) must be a delicate balance to facilitate the MEP but inhibit the reflex activity. This also stresses the need for good antinociception at the spinal level to further block the afferent limb of the reflex movement pathway.

Each of these anesthetic goals can be accomplished using a mixture of agents acting at different neural sites. It is currently believed that anesthetic agents act through their interaction with specific synaptic receptors. The two major categories of action include facilitating the inhibitory effect of gamma-aminobutyric acid (GABA) by actions at the GABAa receptor and the inhibition of the major excitatory synapse at the *N*-methyl-D-aspartate (NMDA) receptor [1]. Other synaptic targets include the neuronal acetylcholine receptor (nACh), the mu opioid receptor, central alpha2 receptors, and the potassium, calcium, and glycine channels [1]. Drugs differ by respective major synaptic targets as well as different subunits of the receptors and the distribution of these receptors throughout the central nervous system. As such, the anesthetic plan is usually developed taking into consideration these goals, the procedural goals (including IOM), and the specific medical issues for each patient. The plan is usually designed for the different phases of general anesthesia: premedication, induction, maintenance, emergence, and recovery.

Phases of Anesthesia

Premedication is the use of medications, usually prior to bringing the patient to the procedure room, to begin an anesthetic effect. Frequently, the patients may receive a small dose of midazolam which contributes to sedation and amnesia. Patients may also receive a short-acting analgesic, such as an opioid, if they are having pain and long-acting analgesics (often non-opioids) to provide postoperative pain reduction, especially in patients with chronic pain. Other medications may also be given to produce various pharmacologic effects such as anti-emesis or antibiotics to reduce perioperative infection. In general, these medications usually have minimal effects on IOM.

Induction is the phase of anesthesia after the patient is brought to the procedure room and basic anesthesia monitoring established (e.g., electrocardiogram, blood pressure, temperature, and pulse oxygen saturation). The doses of induction medications are rather large because of the needed initial cortical and brainstem drug effects; hence, the loss of the cranial nerve mediated blink reflex to eyelash stimulation is used to identify adequate brainstem drug effect. They also serve to load the patient with medications to start accomplishing the anesthesia goals and cover the gap until the maintenance medications are established. Unless an awake intubation or an inhalational mask induction is planned, induction usually includes a sedative drug like propofol, an opioid, and a muscle relaxant to facilitate intubation. These bolus doses would normally preclude IOM monitoring during induction; however, the time needed to establish IOM is such that most of the effects of the induction drugs will resolve except for muscle relaxant effects if longer acting agents are chosen.

If an awake intubation is chosen, the doses of sedative agents and opioids are usually smaller such that a clinical neurological assessment is often possible and IOM can be established sooner. Generally, muscle relaxants are not needed for an awake intubation, but topical application of local anesthetics to the airway may preclude assessment of electromyography of the vocalis muscle.

If an inhalational "mask" induction is chosen, the patient is asked to breathe sevoflurane with or without nitrous oxide. After the patient is asleep and an intravenous line established, the sevoflurane can be reduced and the anesthetic converted to the desired maintenance agents. Since the dose of sevoflurane is rather large, IOM will be affected until the agent has been reduced in the nervous system, which will be somewhat longer than the decrease of the concentration in the breathing circuit as shown on the anesthesia monitoring systems.

Once induction is accomplished, anesthesia is converted to the **maintenance phase**. Two basic types of anesthetic agents are used for maintenance: inhalational and intravenous. Further, combinations of agents are often used in order to accomplish the four main anesthetic goals described above. The choice of these agents has a major impact on IOM such that the integration of patient needs, procedure needs, and IOM considerations must be balanced. During the maintenance phase, slow changes in IOM are typically observed. Although referred to as "anesthetic fade," this may relate to a variety of pharmacologic and other factors [2].

At the conclusion of the maintenance phase is **emergence**. This is the period when the anesthesia is reduced until the patient awakens and is extubated. This requires the resumption of spontaneous breathing and the return of protective airway reflexes. The goal is to have the patient safely awaken so they have a stable physiology and can be transferred to the care of a nurse in recovery phase in the postoperative care unit. Aside from insuring adequate pain relief and minimizing the chance of nausea and vomiting, the major goal is to have the patient awaken promptly to allow a neurological examination to identify problems. Since intravenous anesthetic agents may take longer to eliminate than inhalational agents, the intravenous agents may be reduced during the latter part of the maintenance phase, often after the conclusion of the procedure, and during closure of the wound, which may result in some expected IOM changes.

Specific Anesthesia Drugs Used for Maintenance

Based on the synaptic targets involved with individual agents, each anesthetic agent contributes differently to the four goals of anesthesia. For example, at clinically (or surgically) equivalent depths of anesthesia, some agents may produce a different spectrum of cortical or spinal cord evoked potential depression than other agents. The differences between drugs may be explained by differing profiles on receptor types (e.g., GABA and NMDA), differing location of drug action (i.e., pre- or postsynaptic effects), the effects on individual subtypes of these receptors, and the anatomic distribution of the receptors and subtypes. The differences between drugs also contribute to different profiles of drug action on monitored responses.

Halogenated Inhalational Agents

The halogenated inhalational anesthetic agents (isoflurane, sevoflurane, desflurane) are the most frequently utilized agents in GA when IOM considerations are not present. These drugs have a broad action on neural structures with excellent cortical effects on actions of unconsciousness and amnesia (action at the GABAa receptor), excellent spinal cord effects leading to immobility (effect at the glycine receptor), some contribution to antinociception (actions at the NMDA, nACh, sodium, and potassium channels), and some muscle relaxation effects (from action at the nACh receptor in the neuromuscular junction). These actions make them very versatile agents that provide excellent coverage for amnesia and immobility which are major concerns of anesthesiologists.

Table 5.2 Properties of inhalational anesthetics

Agent	Adult MAC (vol%)	Blood:gas Partition Coefficient
Isoflurane (Forane®)	1.15 %	1.4
Sevoflurane (Ultane®)	2.1 %	0.68
Desflurane (Suprane®)	6 %	0.42
Nitrous oxide	105 %	0.46

Data taken from [3, 4]

These agents are modern relatives of ether that are liquids which can be vaporized and mixed into the anesthetic breathing circuit for delivery to the patient. They are relatively inexpensive and very easy to deliver and adjust. Aside from physical chemical characteristics, the three currently commonly used agents differ in their potency, solubility in the body, and pungency. Their potency is typically measured by the minimal alveolar concentration in the lung where 50 % of subjects move (and the other 50 % don't) to a painful peripheral stimulus. This value, in volume %, is termed "MAC," and typical values are shown in Table 5.2. Of note these values decline with age such that a given concentration may have a more profound effect in older individuals. There also are a number of states, conditions, and medications that can increase or decrease MAC requirements (e.g., chronic alcoholic increase MAC, pregnancy, decrease MAC, etc.)

In general, since the different agents act through similar neural mechanisms, the agents are thought to be equivalent when compared at concentrations of similar MAC value. Hence, 1 MAC of desflurane is considered approximately equivalent to 1 MAC of sevoflurane such that substituting one for the other (such as for pungency or solubility) should have similar effects.

The second property, solubility in tissues, is the basis for the time it takes to raise and to lower the anesthetic effect in the body. This is reflected in the blood: gas partition coefficient, where a higher coefficient is a more soluble agent (Table 5.2). Although raising and lowering depends on the mechanics of the breathing pattern and cardiac output, a drug which is least soluble (e.g., desflurane) has its concentration in the brain rises the quickest and reduces the quickest when the delivery is stopped. For this reason, many anesthetists favor desflurane (quickest) or sevoflurane (second quickest) over isoflurane (least quick) when wanting to use an agent with IOM that might need to be eliminated because of excessive IOM effects.

Finally, pungency is the property of irritation of the lung when breathing the agent. Of these three agents, sevoflurane and nitrous oxide are the least irritating so that if anesthesia needs to be induced by having the patient breathe the agent (i.e., there is no intravenous line), sevoflurane (with or without nitrous oxide) will be the choice. Isoflurane and desflurane are simply too irritating to be practical for mask induction.

Since the halogenated agents have broad actions at many synaptic targets, they provide a model for understanding the effect of anesthetic agents on IOM modalities. In summary, since the effects occur at synapses, the location of synapses in the IOM pathway will help explain the resultant effects.

As such, the somatosensory evoked potential (SSEP) has minimal anesthetic effects on the responses recorded from the peripheral nerve and spinal cord since the first synapse is located at the cervical-medullary junction. Since a second synapse is located at the thalamus and the remainder in the primary sensory cortex, the most prominent anesthetic effects will be on responses recorded from the cortex. This is shown in Fig. 5.1. Of interest is that the change in cortical amplitude is nonlinear similar to the "on–off" nature of anesthetic effect on consciousness. This is consistent with an anesthetic effect producing a blocking of sensory transmission through the thalamus as postulated by John in his theory of anesthetic action [5]. This is consistent with the practical observation that the inhalational agents must be limited to 0.5–1 MAC in order to monitor the cortical SSEP. Since patients will vary with their actual anesthetic effect (50 % will be higher or lower than the average MAC), this "on–off" concentration may be higher or lower than reflected in the average value. Further, some pathologic processes may predispose the patient to a more profound effect, suggesting some patients may not have recordable IOM responses with any concentration of the agent.

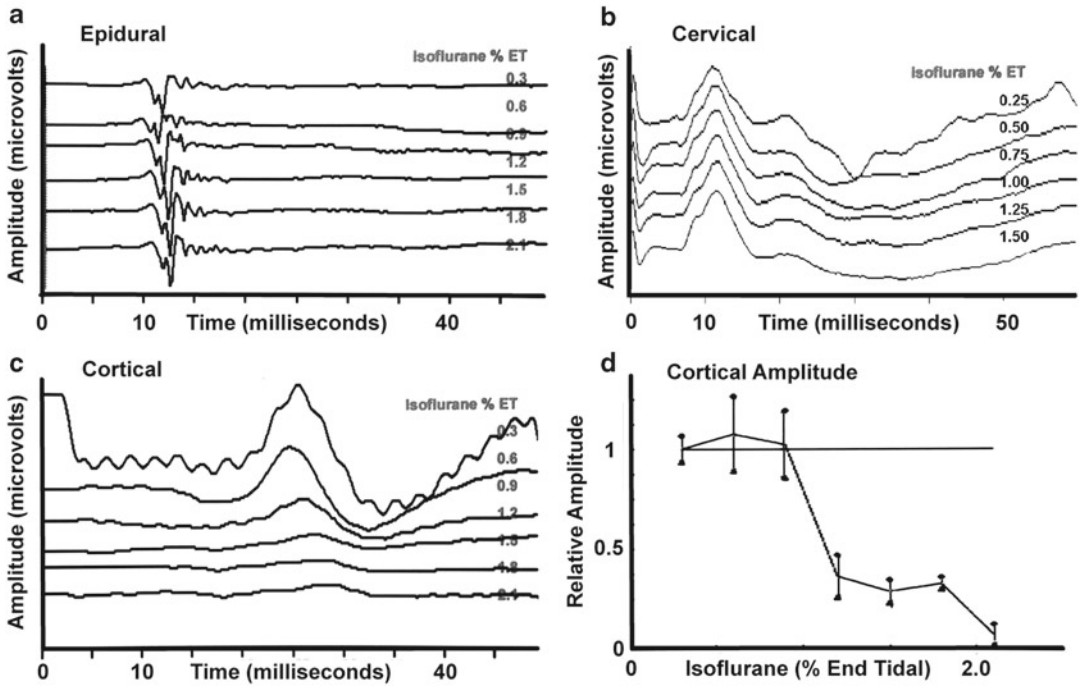

Fig. 5.1 Effect of isoflurane on SSEP recordings. Changes in lower extremity somatosensory evoked potentials recorded at several locations with increasing concentrations of isoflurane in the baboon. (**a**) Shows recordings from the epidural space that indicates minimal effects. (**b**) Similarly shows minimal effects in the response recorded over the cervical spine. (**c**) Shows a prominent effect on the response recorded over the somatosensory cortex. (**d**) Shows a plot of the amplitude of the cortical response demonstrating a nonlinear amplitude reduction as the isoflurane concentration is increased. Reproduced from Sloan with permission [70]

The cumulative anesthetic effect on synapses is also seen with the brainstem auditory response (waves I–V) which shows a progressive increase in effect as the number of synapses increases along the auditory pathway (V > III > I) (Fig. 5.2). Also similar to the SSEP, the cortical auditory response (mid-latency auditory evoked potentials, MLAEP) is markedly affected. The effect on the cortical visual evoked response is also substantial consistent with the multiple synapses involved in the cortical response.

The location of synapses in the motor pathway is consistent with the dramatic anesthetic sensitivity of transcranial motor evoked potentials. Since these responses are elicited by direct stimulation of the motor cortex which produces a "D" wave recorded near the spinal cord and no synapses are involved, the D wave is resistant to increasing doses of halogenated agents (Fig. 5.3). However, since the "I" waves recorded near the spinal cord are produced by transynaptic stimulation in the motor cortex, their loss is consistent with anesthetic effect on cortical synapses (Fig. 5.3).

The second location of synapses in the motor pathway is in the spinal cord gray matter where descending motor pathways activate peripheral motor nerves. At this location, the number of synapses varies with the specific muscles; however, the more proximal muscles have more synapses, suggesting why the more distal muscles in the limbs may provide the best recording sites during anesthesia.

The production of peripheral motor responses results from the cumulative effect (temporal summation) of D and I waves and anterior horn cells. As such, the loss of I waves explains why the single-pulse transcranial stimulation of the electrical or magnetic technique is so exquisitely sensitive to anesthesia and why the high-frequency multipulse technique is more successful since it produces

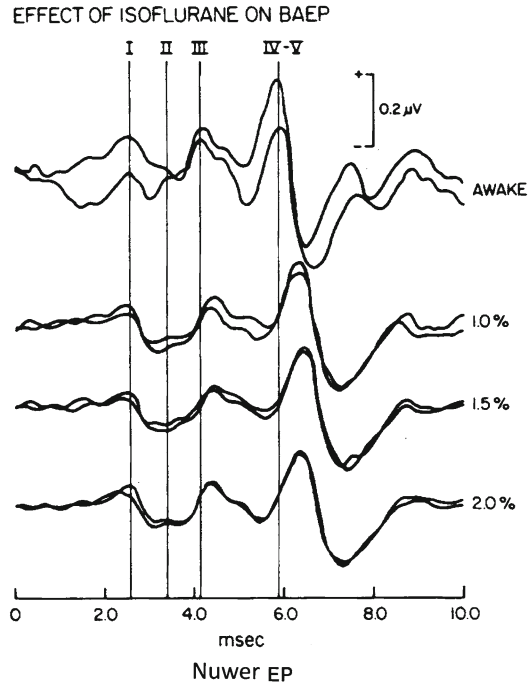

Fig. 5.2 Effect of isoflurane on auditory brainstem response. Influence of isoflurane on auditory brainstem response (ABR). Latency of peaks III and IV–V is progressively increased with increases in isoflurane. The effect on IV–V is more than on III. Reproduced from Manninen with permission [71]

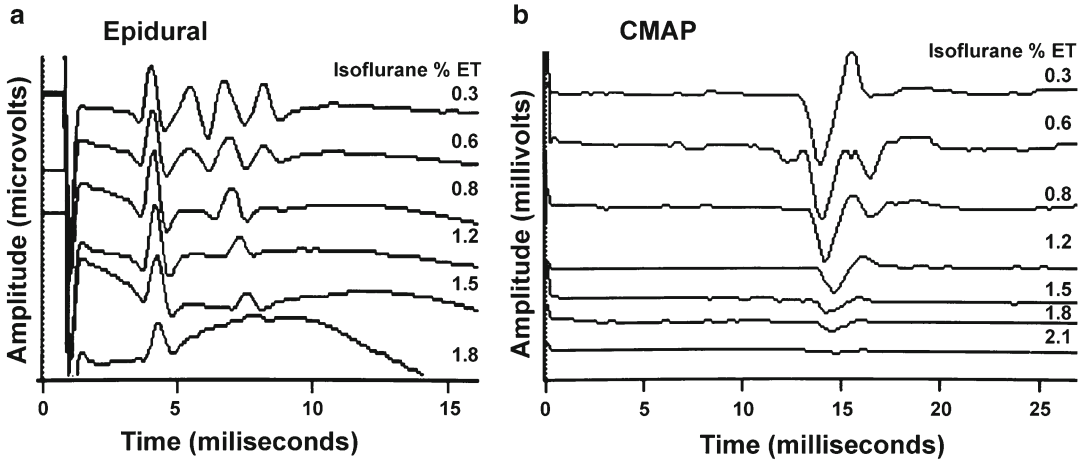

Fig. 5.3 Effect of isoflurane on motor evoked potentials. Changes in transcranial motor evoked potentials recorded in the epidural space (**a**) and in compound muscle action potentials (CMAPs) in the hand (**b**) in the baboon. Shown is the maintenance of the single D wave ("D") and loss of the multiple I waves ("I") in the epidural recording and loss of the CMAP response with increasing concentrations of isoflurane. Reproduced from Sloan with permission [70]

multiple D waves that can summate more successfully. However, anesthetic effects at these spinal gray synapses can block the production of peripheral motor responses. In addition, a variety of other descending tracts (descending suprasegmental systems [corticospinal, rubrospinal, vestibulospinal, and reticulospinal systems] and propriospinal systems) influence the excitability of the anterior

horn cells such that anesthetic effects on these pathways may also hamper the production of muscle responses. Thus, the cumulative effect of the cortical and spinal synaptic effects may explain why the muscle responses from transcranial stimulation are so easily affected by anesthetic agents.

It is of interest to note that the effects of the anesthetic agents on the spinal gray matter form one of the anesthetic challenges for the choice of agents. Clearly, the ability of a descending motor pathway impulse to produce a motor nerve response or the muscle response follows the same pathway which needs to be blocked to prevent patient movement in response to peripheral noxious stimuli such as surgery. Thus, a balance of effects is needed, and contributions of anesthetic agents, which block noxious stimuli coming into the spinal cord, are important to block the reflex pathway leading to immobility. Perhaps the profound effect of the halogenated agents on the reflex activity mediated through the glycine channels explains why this balance is difficult to achieve in their presence.

Similar to the SSEP, the MEP response also shows a nonlinear loss over a narrow anesthetic concentration. This means that some individuals will have muscle responses that can be acquired with 0.5 MAC of an inhalational agent, but most will require a careful titration of intravenous agents (TIVA). For these many reasons, the anesthetic effects on the motor pathway make the muscle responses of the transcranial motor evoked potential one of the most difficult monitoring techniques under anesthesia.

The anesthetic effect of the halogenated agents in the spinal cord accounts for the depression of the H-reflex. Studies of the anesthetic effects on the H-reflex show that it parallels the movement to noxious stimuli used to measure MAC of the halogenated agents. Thus, the anesthetic effects on the motor evoked potentials will mirror the effects on the H-reflex [6].

There is one additional synapse in the motor pathway located at the neuromuscular junction. Although the inhalational agents do have effects at this location, the effects do not appear to be clinically significant in the absence of neuromuscular blocking agents (NMBA). However, the effect of the NMBAs is known to be amplified by halogenated inhalational agents such that the NMBA management must be carefully monitored in their presence such that the motor response is not excessively depressed. Fortunately, the only anesthetic agents that impact the muscles responses from peripheral nerve stimulation are neuromuscular blocking agents and local anesthetics blocking conduction in the nerve.

In summary, the halogenated inhalational agents have broad spectrum of anesthetic effects (i.e., multiple synaptic targets) that provide excellent cortical effects on consciousness and amnesia and excellent effects on the spinal gray matter producing immobility such that they are superb anesthetics when IOM is not being utilized. Since they have less profound antinociception, they are often supplemented with opioids, creating what is often termed a "balanced" anesthetic. However, because of the profound depression of the SSEP and MEP, these agents must often be restricted or avoided during IOM and other agents utilized.

Nitrous Oxide

Nitrous oxide is also an inhaled agent. Nitrous oxide (N_2O) is different from the halogenated agents consistent with anesthetic action at different synapses. N_2O is particularly effective in antinociception due to its action at the NMDA receptor with additional actions at the mu opioid, nACh, and potassium channels. In addition it contributes to unconsciousness and amnesia through minor actions at the GABAa and central alpha2 receptors and contributes to immobility through minor actions at the glycine receptor [7]. In summary, it has excellent qualities in blocking noxious stimuli but weak properties in producing cortical effects (unconsciousness and amnesia) and immobility. This makes it a nice complement to the halogenated agents and explains the logical combination of the two classes in general anesthesia.

The effects of nitrous oxide on the SSEP and MEP are similar to the halogenated agents. However, the potency of N_2O (MAC > 100 %) limits this effect. When compared at equi-MAC anesthetic concentrations, nitrous oxide produces more profound changes in the muscle recordings of motor evoked potentials than the halogenated

inhalational anesthetic agents [8]. Some studies have suggested that similar to low concentrations of the halogenated agents, nitrous oxide may be acceptable for MEP monitoring with multipulse stimulation techniques; however, the other anesthetics used with it make a difference in the degree of depression [9–11]. As such, if only one inhaled agent is to be used, many anesthesiologists would prefer the contribution of the halogenated agents to the cortical and immobility effects rather than the contribution of nitrous oxide to antinociception (which could be accomplished using opioids with less impact on the responses).

Unfortunately for IOM, the combination is synergistic such that the depression of the combination is more profound than would be predicted by the effect of the individual agents [12]. Thus, it is not recommended to use a combination of halogenated agents and nitrous oxide with IOM.

Intravenous Anesthetic Agents

Since the inhaled agents may need to be reduced in concentration (or avoided) in some patients during some IOM modalities (notably transcranial motor evoked potentials and cortical somatosensory evoked potentials), anesthesia maintenance may require the use of intravenous anesthetic agents since these are often more compatible with accomplishing the four anesthesia goals and facilitating IOM. The intravenous agents are usually chosen such that the mixture of agents accomplishes the goals of anesthesia while minimizing the impact on the IOM responses. When general anesthesia is provided solely by intravenous agents, it is termed total intravenous anesthesia (TIVA).

Agents Used to Produce Unconsciousness and Amnesia

One key class of intravenous agents is those which contribute effectively to unconsciousness and amnesia. Referred to as sedative, hypnotic, and amnestic agents, these include propofol, etomidate, dexmedetomidine, and midazolam (Table 5.3).

Table 5.3 Commonly used sedative, hypnotic, and amnestic intravenous agents

Agent	Trade name
Propofol	Diprivan®
Etomidate	Amidate®
Dexmedetomidine	Precedex®
Midazolam	Versed®

Propofol

Of these agents, propofol is currently the most commonly utilized sedative and amnestic agent. Propofol has potent effects via actions at the GABAa receptor which increases the inhibitory effects of GABA, acts at extrasynaptic GABA receptors, and has some action at neuronal nACh receptors. This action at the GABAa and minor effects at the glycine receptor in the spinal cord contribute to immobility during anesthesia. Finally, it makes minor contributions to antinociception through minor actions at the glycine and nACh receptors. At the spinal cord level, the dose–response curve for reflex movement is substantially flattened compared to the halogenated agents such that a dose can usually be found that provides adequate suppression of movement without the depression of the MEP seen at higher doses [13].

Propofol does have depressant effects similar to the halogenated inhalational agents. For this reason (as with all anesthetic agents), a constant infusion is required to prevent sudden changes in drug concentration that depress the IOM responses simulating neural compromise. Usually a dose can be chosen which produces the desired anesthetic effects without excessive depression of the IOM responses.

At higher doses, it will block the responses such that if they are needed for an individual patient, other agents may need to be added to accomplish the cortical effects and reduce the propofol dosage. One of these agents is ketamine which is discussed below [14]. A second, less commonly used agent is an infusion of lidocaine which also reduces the dose of agents used for antinociception [15, 16]. A newer version of propofol named fospropofol does not appear to have any advantages over propofol [17].

Propofol is used as a common induction agent for anesthesia (usually in doses of 1–2 mg/kg). With TIVA, the initial bolus dose is needed to get the blood level up to the needed dose so that a subsequent infusion can keep the needed effect level. That infusion is designed to match the metabolism or clearance of the drug so that a constant drug level is maintained to provide the needed level of anesthesia and a constant level of drug effect on the monitoring. In general, this infusion rate will vary with the patient needs but is usually 120–180 μg/kg/min when it is used solely with an opioid in TIVA. The infusion may be higher in patients who need a higher effective blood level because of drug tolerance from preoperative medication usage or may be lower when other medications are added to the TIVA that also provide some sedative-hypnotic effects (e.g., inhalational agents or lidocaine infusions). As with all of the anesthetic agents, a constant level is important to minimize acute changes in the monitoring.

Etomidate

An alternative sedative/hypnotic to propofol is etomidate, which also has potent effects on unconsciousness and amnesia via actions at the GABAa receptor. An advantage is that etomidate has limited cardiopulmonary depressant effects and has a role during induction in selected patients. It contributes to immobility via actions at the GABAa and glycine receptors and has some minor contributions to antinociception through actions on the potassium channels. Many practitioners have avoided etomidate in infusion over time because of concerns of worsened outcome in patients with sepsis secondary to the depression of corticosteroid production in the adrenal gland [18, 19].

Etomidate is unusual because at clinically useful doses it enhances the EEG and increases the amplitude of both sensory and motor evoked responses [20–25]. This enhancement may produce seizures in patients with epilepsy; the combined effect of enhanced activity of epileptic foci and transcranial electrical stimulation is unknown [26].

Etomidate is delivered similar to propofol in bolus doses for induction and by infusions for TIVA. Its use for induction as a bolus (typically 0.2–0.3 mg/kg) is often favored in patients who may be dehydrated, in the elderly, have poor myocardial function, or who may be hemodynamically unstable because it has less depressant effects on the heart. Similar to propofol, the induction bolus can achieve effective blood concentration so that a subsequent infusion can maintain the effective level for anesthesia. At present, infusions of etomidate in TIVA are limited as indicated related to adrenal suppression. Current research with chemical relatives (e.g., methyl-carbonyl etomidate) may hold promise for an alternative without adrenal depression in the future [17].

Benzodiazepines

Prior to the introduction of propofol (and prior to MEP monitoring), an infusion of midazolam was used with TIVA [21, 27]. The benzodiazepines, notably midazolam, also act at the GABAa receptor producing amnesia at doses that are not associated with unconsciousness. This produces a mild depression of cortical SSEP and as a premedicant or occasional supplement in anesthesia allows MEP recording [24, 27–32]. In addition to possible cortical locations for the benzodiazepine effect, an effect at the spinal cord has been described as antinociceptive through actions at the GABA receptors in lamina I and II in the dorsal horn [33, 34].

The superb anxiolytic and amnestic qualities make midazolam an excellent addition to anesthesia, but a prolonged drug half-life makes it less favorable than propofol for a TIVA infusion-based anesthetic. As such midazolam is frequently given preoperatively for reduction of anxiety (anxiolytic) and as a method to help insure amnesia when concerns are raised about the possibility of awareness. These small doses, given intermittently, do not appear to have a detrimental effect on monitoring; however, higher doses have been associated with MEP depression. It is also an excellent agent to add at the

end of a procedure if delirium on awakening is anticipated or to mitigate hallucinatory effects of ketamine (see below).

Dexmedetomidine

One of the newer additions to the sedative agents is dexmedetomidine which acts as a central, selective alpha2 adrenoreceptor agonist drug. It has been shown to reduce the amount of propofol, opioids, and halogenated inhalational agents needed during maintenance [35]. The sedative drug effect is primarily due to action in the brainstem (locus coeruleus) which decreases cortical arousal influences producing sleep similar to normal sleep. Although not FDA approved at present for use in general anesthesia, it is approved for sedation in the intensive care unit where patient awakening allows a less effected neurological exam. Of note it does not appear to have amnestic action. Side effects of hypotension and bradycardia occur as a consequence of effects on the brainstem limit the drug to a role as a supplement to other anesthetic agents.

Dexmedetomidine has "opioid-sparing" properties and appears to be an excellent supplement in the opioid-tolerant patient. The effects on SSEP recordings are minimal but, as with propofol, higher blood levels of dexmedetomidine (or when moderate dosages of other agents such as propofol are used with dexmedetomidine) inhibit MEP monitoring making its use challenging [36, 37].

Dexmedetomidine is not used as a sole agent in TIVA for two reasons. First, its dose is limited because it reduces the sympathetic influences from the brainstem which results in bradycardia and hypotension. Second, at acceptable doses, it does not produce adequate antinociception and amnesia so these effects must be provided by other medications. Hence, TIVA can be accomplished by dexmedetomidine infusion supplemented by low-dose propofol for amnesia and an opioid infusion for antinociception. Alternatively, a low-dose inhalational agent may be used instead of the propofol to provide the amnestic action. Often these combinations will be acceptable for SSEP recording but, if higher doses of dexmedetomidine or propofol are used, MEP monitoring may not be possible.

Intravenous Agents Used to Block Noxious Sensory: Antinociception

Intravenous agents must also be chosen to block noxious sensory stimuli. These drugs will assist in immobility by blocking the afferent limb of spinal reflex activity if the agents work at the spinal cord as well as reducing sensory stimuli to the brainstem and cortex which increase the need for sedative and amnestic agents. The primary agents used with TIVA include the opioids and ketamine, although dexmedetomidine and lidocaine infusions also contribute to the antinociception (Table 5.4) [38].

Opioid

Infusions of opioids have mild effects on evoked responses while producing excellent antinociception by actions in the dorsal horn of the spinal cord, at multiple sites in the cerebral cortex and brainstem, and in the rostral ventromedial medulla which is responsible for a descending modulatory system which modulates processing of noxious stimuli in the dorsal horn. The naturally occurring opioids (e.g., morphine) have some sedative properties; however, the agents usually used with anesthesia (fentanyl, sufentanil, remifentanil) do not have significant sedative or amnestic properties. As such, opioids (e.g., fentanyl, sufentanil, remifentanil) form an important component of TIVA as they can have mild effects on monitored responses. Opioids can potentiate the effect of propofol and suppress

Table 5.4 Commonly used intravenous agents for antinociception

Agent	Trade name
Fentanyl	Sublimaze®
Sufentanil	Sufenta®
Remifentanil	Ultiva®
Ketamine	Ketalar®

motor reflexes and spontaneous activity. In addition, bolus doses of these agents will produce transient depression of responses, and higher concentrations can persistently produce significant depression such that delivery of the opioid by infusion is important during anesthetic maintenance similar to the use of infusions of agents use for unconsciousness and amnesia [39]. Unfortunately opioids do not produce unconsciousness or amnesia and may be less effective in opioid-tolerant, chronic pain patients.

Ketamine

As an alternative or supplement to the opioids, ketamine has very potent antinociceptive actions via its action at the NMDA receptor. Ketamine is also thought to act by inhibition of the neuronal nicotinic acetylcholine receptors, decreasing the presynaptic release of glutamate, and through opioid-like actions on the opioid receptors. Ketamine can be particularly effective in the opioid-tolerant patient.

In addition, it contributes to unconsciousness and amnesia via minor actions at the GABAa receptor. Like etomidate, ketamine is an excitatory agent and has been reported to increase cortical SSEP amplitude [40, 41], increase the amplitude of muscle and spinal recorded MEP responses, and increase the H-reflex [42–44]. Because it has cortical effects, ketamine can be added to an intravenous technique to enhance the antinociceptive effect while allowing reduction of agents which produce depression of the evoked responses such as when high doses of propofol would otherwise be needed. Unfortunately, increases in intracranial pressure in patients with cortical abnormalities or hallucinatory activity limit its usefulness. The latter effect can lead to a delirium on emergence with subsequent unfavorable effects similar to post-traumatic stress. The latter can be minimized by avoiding ketamine during the conclusion of the procedure (which may lead to an amplitude reduction of the SSEP and MEP) or the utilization of midazolam at awakening. Fortunately, the hallucinatory effect of ketamine in children is less than adults making it a common choice in children. As such, ketamine is often given early in a procedure (such as at induction), by intermittent boluses or by a low-dose infusion with avoidance of the drug during the last hour of the procedure.

Lidocaine

An additional agent that is reemerging as a supplement to provide antinociception is intravenous lidocaine. At the low-dose infusion used with TIVA, it contributes to sedation, antinociception, and immobility in TIVA. As such it reduces the doses of propofol and opioids needed [45–47]. It is postulated that the cortical actions occur primarily by potentiating GABAergic acting agents and NMDA antagonism [45, 48–50]. The contribution to antinociception is thought to occur at the spinal cord and cortical levels with the antinociceptive action contributing to immobility by blocking the afferent noxious stimuli.

Agents Used for Immobility

As indicated above, the agents used for antinociception, unconsciousness, and amnesia also have effects at the spinal cord level reducing the afferent sensory limb or reflex arc in the spinal gray matter leading to immobility. Achieving this delicate balance is one of the major challenges with TIVA.

Neuromuscular Blocking Agents

A second method of producing immobility is the use of neuromuscular blocking agents to reduce transmission across the neuromuscular junction. As mentioned above, these agents are often used to facilitate intubation at induction and may be requested during certain procedure periods such as during abdominal exposure of the spine or during separation of the posterior musculature from the spine during a thoraco-lumbar corrective surgery. If neuromuscular blockade is utilized during the portion of the procedure where IOM using

Table 5.5 Drug doses and effects of commonly used neuromuscular blocking agents

Drug	Intubating dose (mg/kg)	Onset (min)[a]	Duration (min)[b]
Succinylcholine	(Anectine®) 1	1	10
Cisatracurium	(Atracurium®) 0.1	2.5	45
Rocuronium	(Zemuron®) 0.6	1.3	33
Vecuronium	(Norcuron®) 0.1	3	33

[a]Time to 95 % depression of a single muscle response to supramaximal stimulation of a nerve
[b]Time to recovery of the single response to 25 % of the unblocked response

muscle responses is desired, a carefully controlled infusion producing a partial neuromuscular blockade is needed.

However, their use during intraoperative electrophysiological monitoring (IOM) using muscle-derived responses (e.g., spontaneous and stimulated electromyography [EMG] and muscle responses to transcranial motor evoked potentials [MEP]) is controversial because they can reduce the amplitude of the responses and simulate loss of neural function. Hence, many individuals recommend their avoidance during the monitoring portion of procedures [51, 52].

These agents block transmission across the neuromuscular junction by interfering with the action of acetylcholine (ACh) released from the presynaptic terminal in response to the depolarization of the peripheral nerve [53, 54]. Currently, the commonly used NMBAs include succinylcholine, vecuronium, rocuronium, and cisatracurium (Table 5.5). Succinylcholine is referred to as a "depolarizing" agent because it stimulates a muscle contraction before blocking ACh action. It is usually rapidly metabolized by plasma cholinesterase which gives rise to its short duration of action (except in a few patients where inherited abnormalities in the enzyme lead to prolonged action up to 4–6 h) [55]. Many anesthesiologists consider succinylcholine the best agent for intubation with an anticipated awkward intubation or where the patient may regurgitate gastric contents on induction.

The depolarizing effect of succinylcholine leads to two undesirable side effects. First, the muscle contractions may lead to unpleasant muscle pain postoperatively. This can sometimes be reduced with pretreatment of a small dose of non-depolarizing agent (e.g., rocuronium). More importantly, the depolarization leads to a potassium efflux that is normally of no consequence, but can be life-threatening (e.g., cardiac arrest, lethal arrhythmia) in some circumstances such as recent spinal cord, neuromuscular disease, or crush injury. Increases in intraocular and intracranial pressure can be seen with succinylcholine. Also it can trigger malignant hyperthermia (as can inhalational agents) in the rare susceptible patient where its use is contraindicated (if known through family history or testing). This inherited condition results in excessive muscle hyperactivity with massive release of calcium from the sarcoplasmic reticulum, which is associated with hyperthermia, muscle breakdown, and consequent life-threatening metabolic derangements which demand immediate cooling and treatment with dantrolene.

The other neuromuscular blocker agents are referred to as non-depolarizing because they occupy the postsynaptic Ach receptor, competitively blocking neuromuscular transmission without causing initial muscle activity. These agents also interact at a presynaptic receptor which reduces the availability of stored Ach leading to reduced Ach release with closely timed stimulation [56, 57]. This latter effect leads to the "fade" seen in the train of four, where each successive response is smaller. The effect of these drugs is terminated through metabolism by the liver and kidney except for cisatracurium which undergoes spontaneous chemical decomposition ("Hoffman elimination"), making it useful when hepatic and renal function is limited or nonexistent [58]. In general, these agents have a slower onset and longer duration of action than succinylcholine but have pharmacokinetics suitable for use by infusion. In general, if an NMBA is needed for intubation, succinylcholine or rocuronium is often chosen to minimize the time to subsequent acquisition to IOM baselines that involve muscle activity.

If needed, the neuromusclar blocking effect of a non-depolarizing agents can reversed, and this typically occurs at the end of a surgical case. The common method of reversal involves increas-

ing the released amount of acetylcholine by preventing its metabolism by an acetylcholinesterase inhibitor (e.g., neostigmine [Prostigmin®]). This agent is administered with an antimuscarinic agent (glycopyrrolate or atropine). Cholinergic receptors are both nicotinic and muscarinic, and unopposed increases in acetylcholine with an acetylcholinesterase inhibitor will help overcome the competitive nondepolarizer blocker; however, there will also be a muscarinic effect, including the potential for bradycardia and even asystole. This reversal can only be effective if the level of blockade has reduced such that the higher amounts of acetylcholine can effectively compete for action at the receptors [59]. Hence, one or more responses in the train of four need to be present before the reversal will succeed, which correlates to no more than 2/3 of acetylcholine receptors being blocked (see below). When it becomes available in the United States, a novel cyclodextrin drug which sequesters rocuronium (sugammadex) may allow reversal of a more profound blockade, without the potential for cardiovascular effects as seen with acetylcholinesterase agents.

Although many practitioners recommend avoiding neuromuscular blockade when IOM techniques utilize muscle responses, partial neuromuscular block has been used. A partial blockade must be titrated in a carefully controlled infusion. The monitoring of the effect is normally done using "train-of-four" paradigm where the EMG response of a muscle is measured following four supramaximal stimulations of a peripheral nerve at 2 Hz. This produces a progressive reduction of muscle responses (fade) in the train of four such that a reduction in the size of the fourth response (T4) to the first response (T1) is seen (train-of-four ratio) that is related to the degree of blockade [60]. Additional blockade causes a reduction in the number of responses until all are gone. The degree of blockade can sometimes be assessed when no responses are present by counting the number of "posttetanic" responses occurring at 1-s intervals following a 5-s tetanic stimulation [61].

Monitoring of the train of four in muscles used for IOM is important because the NMBA can cause different degrees of blockade in different muscles and the muscles chosen by the anesthesiologist may not represent those used for IOM [61]. For example, the most peripheral muscles (hands and feet) are blocked at drug levels below that which block more proximal and truncal muscles. The diaphragm requires the highest drug level such that a patient may be breathing or coughing when distal muscles are completely blocked. As the blockade resolves this, and other differences in muscle sensitivities, gives way to a nonuniform resolution of blockade stressing the need to monitor TOF individual muscles involved in monitoring to be sure the individual muscle status is known. Further, a variety of factors can alter the usually expected response to NMBA. These include hypothermia and a variety of medications, including antiepileptic agents [61].

When neuromuscular blockade is utilized, MEP and muscle responses secondary to cranial nerve or peripheral nerve stimulation have been successfully monitored when the train of four has two responses [61, 62]. When monitoring is being utilized to detect nerve irritation by mechanical or other nonelectrical stimuli, the amplitude of the response will be reduced by the blockade, but no studies have been done to clarify the exact reduction or any recommendations for acceptable neuromuscular blockade. Hence, in these circumstances, many individuals recommend avoiding neuromuscular blocking agents.

Physiological Management

The anesthesiologist monitors and manages the physiology of the patient. Often the management maintains the patient physiological parameters in their normal range. The various monitors used can be helpful to the IOM team to determine physiological factors that may be contributing to alterations in the IOM responses. Sometimes, the physiology is intentionally altered (e.g., deliberate hypotension or deliberate hypothermia). Blood pressure management is particularly important as it is a major determinant of tissue blood flow. In normal tissue, cerebral and spinal cord blood flow is thought to be "autoregulated" such that over a range of blood pressures, the

blood flow is maintained constant. Mean pressures below the "lower limit of autoregulation" result in below normal blood flows which may compromise tissue flow if it is below the normal margin of safety. In the past this lower limit was thought to be 60 mmHg, but a reappraisal of the studies has suggested it is variable and a more representative average value is 70 mmHg with some patients having lower limits above that level [63–65].

This autoregulation has been used to support the use of deliberately lowering the blood pressure (deliberate hypotension) so as to reduce the blood loss during spine surgery or reduce the risk of intracranial aneurysm rupture. In many patients, particularly young healthy patients, this lowering has been conducted with no significant risk to the spinal cord or brain. However, if the nervous system becomes compromised (e.g., ischemia), or the patient autoregulates at higher pressures (such as a patient with hypertension), the patient may require a higher pressure to insure adequate blood flow and health. Hence, excessive hypotension can lead to ischemia, and SSEP changes have been observed at blood pressures which would not ordinarily be associated with neural ischemia (e.g., systolic blood pressures above 90 mmHg systolic). Hence, changes in the SSEP and MEP may signal the need to raise the blood pressure such that the monitoring may help the anesthesiologist adjust the blood flow to reduce neurological risk [66–69]. In addition to global hypotension, regional hypoperfusion (e.g., obstructed artery to a limb), hypoxemia, severe anemia, excessive hyperventilation, and reduced neural perfusion pressure (e.g., raised intracranial or cerebrospinal fluid pressure) can lead to ischemia.

With respect to blood pressure and blood flow, it is important to note that patients may have regions of poorer perfusion or vascular anomalies that can compromise blood flow. For example, the cortical regions at the boundaries of the anterior, middle, and posterior cerebral arteries are more sensitive to reductions in arterial pressure that the middle of the vascular regions (especially the triple boundary zone at the junction of the three regions). Similarly the low cervical-high thoracic region of the spinal cord is another "watershed" area which has a precarious blood supply at the boundary of perfusion from the vertebral and cervical arteries and from the more caudal segmental radicular perforators from the aorta. This region has been known to become ischemic with excessive flexion of the neck in the sitting position. Finally, normal variants of the vasculature may not be known in individual patients (e.g., interruptions in the circle of Willis in the brain and variations in the location of the artery of Adamkovich or segmental spinal perforators from the aorta to the spinal cord) such that monitoring may assist in identifying unexpected central nervous system ischemia.

The effect of blood pressure and ischemia on cortical and spinal cord neural tissue also includes a time element. As shown in Fig. 5.4, as cerebral blood flow falls below normal (50 cc/min/100 g), tissue blood flow does not fall until about 18–20 cc/min/100 g indicating a normal margin of safety in the brain. Below this level, the electrical activity becomes abnormal and absent at 12–15 cc/min/100 g corresponding with the blood flow reduction is an increased risk of neural injury which has a time element. This, at blood flows where the electrical activity is altered it may take 3–4 h before a permanent neural deficit occurs. The time to injury becomes shorter as the blood flow is reduced further. Hence, the loss of electrical activity is an early warning sign when ischemia is occurring and usually signals the desirability of maneuvers to increase blood flow. Hence, it is quite common for the anesthesiologist to increase the blood pressure to improve tissue flow when the evoked responses are altered.

Body temperature is commonly below normal in the colder climate of procedure rooms. This can also alter IOM resulting in increases in latency and decreases in amplitude of evoked responses. Like reduced blood flow, hypothermia can also be regional (e.g., a cold limb from rapid infusion of cold fluids or cold spinal irrigation fluids). Although excessive hypothermia has adverse consequences (e.g., increased operative bleeding, postoperative infection, and cardiovascular complications), it is usually not directly detrimental to the nervous system. Changes in other physiological variables

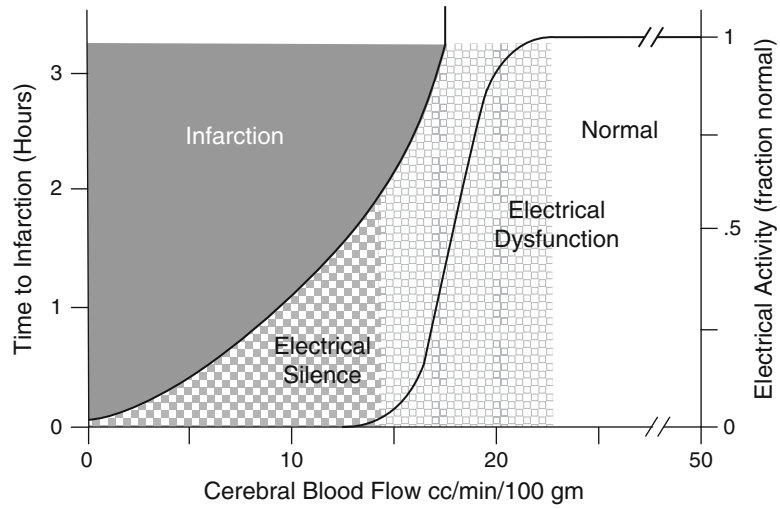

Fig. 5.4 Interaction of cerebral blood flow, electrical activity, and time to infarction. Depiction of electrical activity and the occurrence of irreversible cell death (infarction) as cerebral blood flow is reduced from normal (50 cc/min/100 g). As shown, the EEG becomes abnormal below 22 cc/min/100 g and absent when blood flow reaches 15 cc/min/100 g. Infarction occurs at 17–18 cc/min/100 g after 3–4 h and at progressively shorter periods when blood flow is below this level. Reproduced from Sloan with permission [72]

may produce alterations in the evoked responses during surgical monitoring. These include oxygenation, ventilation, and other factors which alter blood flow or the neural environment. As such, the monitoring conducted by the anesthesiologist can be invaluable to understand global physiological factors which may contribute to and help reduce neural compromise. When regional physiological effects intervene, it may take a concerted effort to identify and correct these factors.

Positioning Considerations

The anesthesiologist also participates in the positioning of the patient for surgery. Occasionally adverse circumstances may result from positioning that is otherwise thought to be adequate or when the procedure results in a change in position leading to neural compromise. Changes in IOM responses may signal a possible compromise leading to a reappraisal and adjustment of the positioning. The procedure team (including the anesthesiologist) actively participates when positioning issues are raised.

Perhaps the most common positioning concerns are raised with the upper extremity where the brachial plexus and peripheral nerves may be stretched or compressed leading to IOM changes. For example, in the supine position, the arm tucked at the patient's side may be pulled towards the feet to improve radiographic images of the lower cervical spine. This may also be coupled with tilting of the head away from that shoulder for better surgical exposure. These positions may stretch the brachial plexus across the head of the humerus or stretch the cervical roots at the spine. With the arm out on an arm board or tucked at the patient's side, concerns are also raised about the ulnar nerve at the elbow from direct pressure on the ulnar nerve and median nerve in the antecubital space from extension of the arm, especially in individuals with muscular arms. When tucked at the side, the sheets used can form a tourniquet or exert direct pressure on the arm similar to the effect of a blood pressure cuff that does not inflate adequately. When out on an arm board, the brachial plexus can be stretched on the head of the humerus by a surgical member or fluoroscopy equipment by pushing the arm excessively towards the head of the table or if the arm falls

towards the floor. Finally, peripheral neural compromise can result from infiltrated intravenous lines (including a compartment syndrome) or a hematoma from an arterial line.

In the prone position, many of the considerations mentioned above also apply. Elevation of the arm above the plane of the body or forcing the arm towards the head of the table can stretch the brachial plexus over the head of the humerus. The ulnar nerve is also at risk from excessive flexion of the arm at the elbow.

Unfavorable positions for the lower extremity appear to be less common, but pressure on the peroneal nerve can occur in the lateral position. In some procedures (e.g., anterior lumbar spine procedures) where cannulas are placed in the femoral artery (e.g., procedures on the thoracoabdominal aorta), a reduction in blood flow to the leg may be confused with neural compression.

Several potential neural compromises are associated with procedures in the sitting position. These include considerations for arm position as noted above, lateral compression of the peroneal nerve from the Mayfield head holder bracket. Monitoring of blood pressure in the extremity when a patient is in the sitting position can patient is in the sitting position can be misleading, with each centimeter of distance from the level of the brain reflecting a difference in true cerebral blood pressure of about 1.3 mm of Hg due to the difference in density of water (approx. 1 g/cm^3) and mercury (13.52 g/cm^3) such that for every centimeter of height correlates with 1.3 mm of mercury. As with any position, neck flexion or extension can lead to spinal cord compression and IOM changes in patients with cervical spine pathology and spinal ischemia in the cervical-thoracic watershed region as mentioned above.

The myriad of positioning-related contributions to IOM changes far exceeds these more common circumstances. Hence, when IOM changes occur, it is important to work with the anesthesiologist to determine if there are position-related issues that could potentially lead to neural injury and interrupt monitoring of the procedure. In addition, resolution of the IOM changes allows the IOM techniques to resume monitoring of the procedure.

Choice of Agents for IOM

As indicated above, a large variety of considerations must be taken into account for the induction and maintenance of anesthesia during procedures where IOM techniques are employed. During the maintenance phase, the anesthesiologist must consider (1) the means to accomplish the anesthesia goals of unconsciousness, amnesia, immobility, and antinociception; (2) accommodating the individual patient's medical and physical needs; (3) the effects of anesthesia on the physiology of the patient; (4) meeting the needs of the surgeon or proceduralist; and (5) trying to provide a favorable environment to facilitate the IOM monitoring. Usually, this will entail a mixture of agents delivered by constant infusion so that fluctuations do not mimic neural compromise.

The considerations for anesthesia with respect to IOM revolve around the techniques employed. In general the modalities can be divided into four categories based on their sensitivity to inhalational agents and sensitivity to muscle relaxants. When more than one modality is used, the effects of the agents must be considered on all of the techniques used.

Those modalities which are insensitive to inhalational agents and muscle relaxants allow the anesthesiologist to choose any of the usual anesthetic agents. These techniques include auditory brainstem responses, peripheral nerve and spinal recorded SSEP responses, and D wave monitoring from transcranial motor cortex stimulation. Interestingly, reduction in muscle tone with neuromuscular blockade may improve the recording of the subcortical SSEP or other areas where underlying muscle activity is reduced.

Those responses that are sensitive to muscle relaxation, but are insensitive to inhalational agents, include the monitoring of peripheral and cranial nerve responses to stimulation or non-stimulated irritation. With the exception of the muscle relaxant considerations, inhalational agents and other anesthetic agents are acceptable. As noted, limited partial neuromuscular blockade

may be acceptable with some of the stimulated techniques, but patients with very small amplitude responses and non-electrically stimulated responses may not be recordable with partial blockade. If partial neuromuscular blockade is used, the challenge for the anesthesiologist is to maintain a stable degree of blockade.

Those responses which are insensitive to neuromuscular blockade but sensitive to inhalational agents include the cortically recorded sensory responses of the SSEP. In these patients, the primary consideration will be restricting the use of inhalational agents such that adequate amplitude responses are present for monitoring. As mentioned, the effect is a nonlinear response with some patients tolerating as much as 1 MAC of inhalational agent and others tolerating little if any agent. In general, since many of these patients tolerate ½ MAC, this dose is often initially chosen using insoluble agents (e.g., desflurane or sevoflurane) that can be eliminated if needed. Since ½ MAC is usually insufficient for anesthesia, infusions of a sedative/amnestic (e.g., propofol) and an opioid are often chosen. In some of these patients, an adjunctive agent (ketamine, dexmedetomidine, and lidocaine) may also be used with or instead of the other intravenous agents. In the net, the tolerance of the neural pathways to cortical depression and the cumulative stimulation and depression of the cortically acting agents determine if the response can be monitored. For these responses, the anesthesiologist can use NMBA which helps to insure that immobility is not a problem.

The most restrictive modalities include the transcranial motor evoked responses because they limit the use of inhalational agents as well as the neuromuscular blocking agents. As such, IOM often requires a total intravenous anesthetic using only mixtures of sedative/amnestic agents and opioids. In these cases, the major challenge (and concern) of the anesthesiologist is to maintain immobility and insure amnesia.

Some adjunctive agents are often helpful (e.g., ketamine) and others appear to be frequently incompatible with recording (e.g., dexmedetomidine). Some patients will tolerate a small dose of inhalational agent (e.g., ½ MAC) but, not infrequently, a pure TIVA will be needed. Of note, the effect of the inhalational agents is nonlinear such that a large drop in amplitude may occur over a small increase in concentration and that threshold varies among patients. Hence, each patient needs to be evaluated individually. In addition, the effect of the agents may change with time as the effect site concentration changes (the intravenous agents in particular) such that a decline in amplitude may occur over time (e.g., this may be the explanation for a time-related "fade" of responses) [2].

Since multimodality monitoring has become standard in most procedures and since motor evoked potentials have become a commonly used technique, total intravenous anesthesia has become a common choice. As eluded to above, some patient variability in the responses will influence the choice of TIVA components and whether a small dose of inhaled agent (e.g., ½ MAC) may be acceptable. In general, very young children (especially under age 2) have incompletely developed nervous systems and therefore are extremely sensitive to anesthetic agents, particularly inhalational agents. In this case, a TIVA technique, often supplemented with ketamine, will be needed for adequate IOM, especially with the use of MEP. In these patients, methods to prime or enhance the motor responses may also be needed (e.g., double burst stimulation or peripheral sensory or motor system priming).

Older age children, especially adolescents, often have robust IOM responses and frequently tolerate supplementation of a TIVA technique with ½ MAC inhalational agent for motor or sensory monitoring. If the child is neurologically normal, this supplementation is often done initially with the caveat that it may need to be eliminated. However, if the neurological exam reveals compromise, it may be better to identify the baselines without the inhalational agent with its addition occurring after good responses are identified.

Adult patients often have less robust responses than adolescents because aging and the effects of medical comorbidities have an impact (e.g., diabetes, vascular disease). Although many adults with normal neurological exams will tolerate ½ MAC inhalational agent, those with myelopathy, weakness, numbness, and tingling may not.

In these patients, baselines with SSEP and MEP are often acquired before the effect of the inhalational agent is assessed. If the responses are excellent, and time allows, a trial of a small dose of halogenated agent is sometimes done. If responses are poor without inhalational agents, ketamine may often be used to enhance the responses and allow a reduction in the propofol dosage.

The most challenging patients are those adults with neurological compromise and chronic pain where the patient is tolerant to anesthetic agents, especially the opioids. In these cases, adjunctive agents may play a key role. Hence, ketamine or lidocaine is often used with SSEP and MEP, and dexmedetomidine used when MEP is not utilized. Since the most common problem with these patients is patient movement, rarely partial neuromuscular blockade is needed.

In general, the anesthesiologist should make the best possible choice of agents based on all of the considerations and then work with the IOM team to identify if the anesthetic can be modified. In some circumstances, the addition of a low dose of inhalational agent may improve the ability to provide anesthesia, while in others, the addition of enhancing agents (e.g., ketamine) to lower or reduce depressant agents may be needed if possible. In any event, a stable constant anesthetic effect is desirable for the critical periods of the procedure so changes in IOM are not caused by changes in the anesthesia agents.

Challenges with Anesthesia

The primary challenges with the delivery of anesthesia rest in the four major anesthetic goals. Unfortunately, there are no accurate methods to titrate the infusions of sedatives, hypnotics, antinociceptive, and drugs used for immobility. Certainly, the occurrence of unexpected tachycardia or hypertension may indicate the effect of catecholamines released by noxious sensory stimulation. Similarly, patient movement may indicate inadequate blocking of the spinal reflexes in response to noxious stimuli. However, effective methods do not exist to determine the adequate doses of drugs to prevent these effects prior to an increase in sensory stimuli. As such clinical experience is often used, and drug infusion doses may be more than needed (contributing to delayed awakening) or less than needed (leading to movement and hemodynamic changes).

Two IOM techniques can, however, provide some assistance. First is observation of the background EMG activity. Since the muscles are normally quiet under anesthesia, EMG activity in multiple channels usually signifies inadequate anesthesia. Second, high-frequency or high-amplitude background EEG activity can assist in suggesting inadequate anesthesia. Unfortunately, there is no uniform effect of anesthetic effects on the EEG, and the EEG only represents a cortical effect that does not always correlate with the drug effects on immobility at the spinal cord level (which often requires a higher dose than the dose for cortical effects). Fortunately, the dose of agents necessary for amnesia is usually below that which produces cortical effects in those drugs which produce amnesia.

Usually, burst suppression in the EEG is suggestive of adequate anesthesia but, as above, the relationship is imperfect. Further, burst suppression is often intentionally produced as a means of lowering cerebral neuronal metabolism to about 50 % of the awake state. Because the cortical neural structures are more sensitive to anesthetic effects, the SSEP can often be recorded despite the inability to use the EEG as a monitor of ischemia when burst suppression is present.

Commercial attempts at producing a processed EEG that represents the degree of drug effect have led to devices to assist anesthesiologists. These might best be described as monitors of "depth of sedation," and many anesthesiologists find them helpful but not completely accurate in predicting adequate drug levels. Thus, during TIVA most anesthesiologists have concern that unexpected movement from inadequate blocking of the spinal reflexes may occur. As such, the use of a small dose (e.g., ½ MAC) of an inhalational agent is often considered desirable when possible. This indicates that the IOM team can partner with the anesthesiologist to find a balance of anesthetic effects on IOM and a satisfactory anesthetic.

Conclusion

The anesthesiologist is clearly an important member of the team to facilitate IOM. Their knowledge of the patient and the pathophysiology of the medical comorbidities are essential to understanding the neural physiology and impact of the surgery and procedure. The choice of anesthesia and management of the physiology is paramount for the success of the IOM. When IOM changes occur, their role is paramount since the etiology can usually be categorized as effects of anesthesia, physiology, positioning, technical, and of the procedure. As above, the anesthesiologist plays a key role helping identifying the possible etiologies and assisting in improving the neural conditions to favor an improved outcome. This emphasizes the close working relationship between the IOM team, the anesthesiologist, and the surgeon or proceduralist.

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Somatosensory-Evoked Potential Monitoring

6

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Somatosensory-evoked potentials (SEPs) are an excellent modality for spinal cord monitoring during surgery. They cover much territory, including the peripheral, spinal, brain stem, thalamic, and cortical levels of sensory pathways. They are used for monitoring for both spinal cord and cerebral injury during various types of surgery.

SEP intraoperative monitoring (IOM) is specific for the dorsal column-medial lemniscal (DCML) pathway but infers protection for other sensory systems as well. Stimulation of mixed peripheral nerves of the upper and/or lower extremity is accompanied by recording from various anatomic generators along the DCML pathway. The posterior tibial nerve (PTN) at the ankle is the most common site for lower extremity stimulation. Alternate stimulation sites include the PTN in the popliteal fossa (behind the knee) or the common peroneal nerve at the knee. Recording sites include a peripheral site at either the popliteal fossa or the spine, a cervical site, and a cortical site (from the scalp). For upper extremity SEP monitoring, the median or ulnar nerves at the wrist are most commonly stimulated with recording sites over the brachial plexus (at Erb's point), cervical spine, and scalp. Figure 6.1 shows an example of stable normal SEPs during a routine case.

The usefulness of SEP IOM is in providing an alert to the surgeon of potential neurological complications in real time, resulting in an intervention that will prevent a negative outcome. SEP IOM may provide the surgeon with reassurance that the surgery is proceeding without complication. This reassurance gives the surgeon the confidence to either complete a procedure or be more aggressive with correction, tumor removal, etc., possibly making the surgery more successful. It is important that information (especially alerts) is given to the surgeon in real time. This allows correlation of the alert with surgical steps that may be undone in order to reverse the change.

Stimulation

SEPs are commonly used in the outpatient lab. In the operating room, the techniques are very similar. Table 6.1 summarizes the parameters used for intraoperative SEPs.

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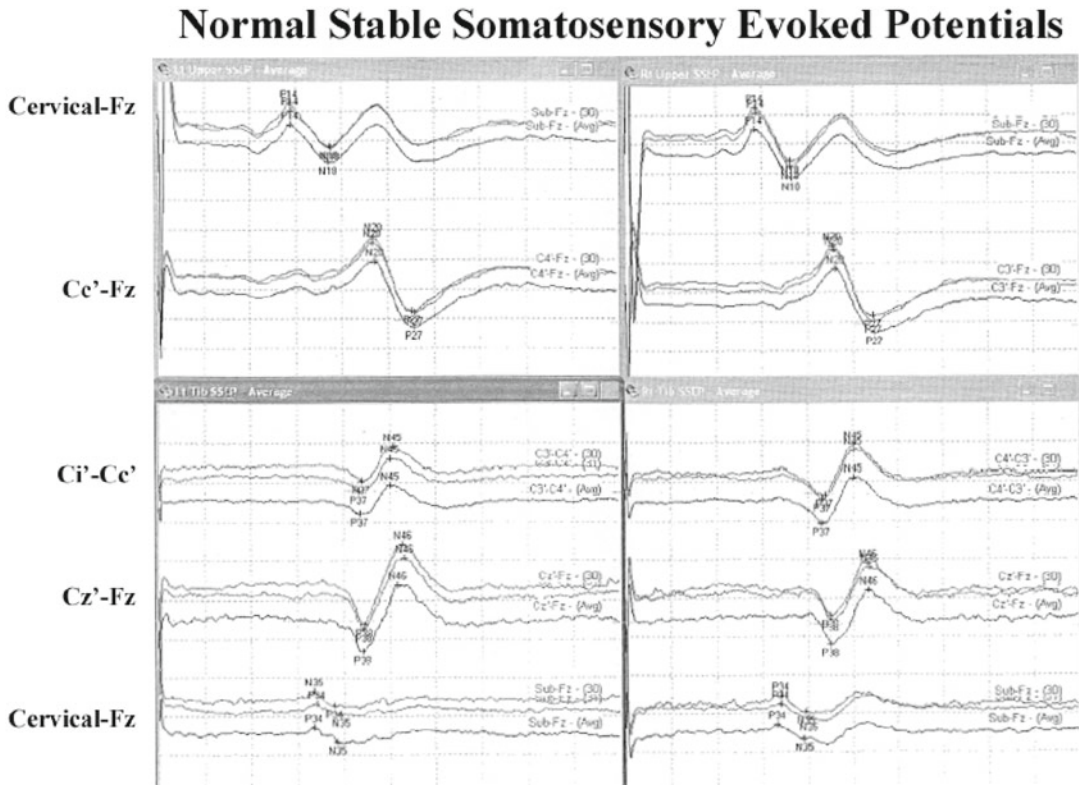

Fig. 6.1 Normal stable SEPs from the left and right median and left and right posterior tibial nerves (From UCLA Dept. Clinical Neurophysiology, with permission)

Sites

For the lower extremities, electrical stimulation to the *PTN* is applied to the ankle. That nerve is superficial and located just posterior to the medial malleolus. For some patients, the *peroneal nerve* is chosen instead. That nerve can be found superficially lateral to the knee just below the fibular head. That site is useful especially in patients with a peripheral neuropathy, such as diabetics, and in the elderly. Stimulation to the upper extremity is delivered to the *median nerve* or *ulnar nerve*. Both nerves are superficial at the wrist.

Peripheral nerves may be stimulated unilaterally to test left and right sides separately. For bilateral monitoring, left and right stimulation can be alternated during the same period of time in a method called asynchronous stimulation. Asynchronous stimulation allows for the rapid collection of data while retaining the ability to interpret data with side-to-side specificity. Modern IOM equipment can average simultaneously from several sites using programmable protocols with delays between different stimulation sites.

Bilateral upper and lower SEP monitoring is used for spine cases. Median or ulnar nerve stimulation is included in thoracic and lumbar cases as a means of monitoring for nonsurgical changes such as anesthesia-related changes. Ischemia secondary to hemodynamic events may also be detected by SEP monitoring from all extremities. Ulnar nerve monitoring also can help detect an incidental brachial plexus impairment resulting from patient positioning during long cases.

For cervical procedures, median or ulnar nerve pathways are the primary pathways monitored. Because the ulnar nerves enter the spinal cord at

Table 6.1 SEP monitoring techniques

Stimulation
Lower extremity stimulation sites
Posterior tibial nerves at the ankle
Or peroneal nerves at the knee, e.g., in patients with peripheral neuropathy
Upper extremity stimulation sites
Median nerves at the wrist for intracranial cases and cervical cases C5 and above
Ulnar nerves at the wrist for spinal cases at or below C6
Stimulus intensity
Supramaximal (10 % over intensity required to record maximal peripheral response)
Stimulus rate
5.1 per second per nerve, if tolerated with good peaks
Or slower if needed to obtain good peaks avoiding harmonics of 60
Recording
For lower extremity stimulations
Two cortical channels, CPi–CPc and CPz–Fpz
A cervical channel: CSp5–Fpz
For upper extremity stimulations
Two cortical channels, CPc–CPi and CPc–Fpz
A cervical channel: CSp5–Fpz
One peripheral channel: Erb's point ipsilateral, contralateral
Filters 30 and 3,000 Hz, notch filter off, adjusting the filters as needed
300 trials per EP, more if needed

a lower level, ulnar nerve monitoring is preferred for cervical cases at and below the C6 spinal level. PTN channels are monitored in cervical cases for detection of a high thoracic or low cervical spinal cord injury. The additional limb coverage also provides greater spinal cord protection from perisurgical events such as hemodynamic changes.

Averaging

SEP data are low amplitude, often <1 μV. This amplitude is less than the surrounding noise field, which includes cerebral activity EEG. For this reason, SEP data must be averaged. Averaging of low amplitude signals increases the signal-to-noise ratio (SNR) in a manner proportional to the number of trials. More trials result in better SNR. About 300 averaged recording trials often produce well-defined peaks.

Intensity

The correct way to determine the optimum stimulus intensity is to determine the intensity that produces the largest amplitude peripheral response and then add 10 %. This is known as supramaximal stimulation and ensures that 100 % of the nerve fibers are being recruited and that small changes in electrode resistance won't appreciably affect the recruitment percentage. Supramaximal stimulation will exceed the motor threshold and cause a 1–2 cm movement in the appropriate muscle groups in the absence of neuromuscular blockade. Median nerve stimuli produce thumb movement. Ulnar nerve stimuli produce fifth digit movement. PTN stimuli produce foot flexion, while peroneal nerve stimuli produce foot dorsiflexion. A stimulus artifact should be seen in the recording channels confirming that the stimulus is actually being delivered. Many modern IOM machines show current delivered and returned, and this is also used for confirmation of stimulus delivery.

Electrodes

Stimulation electrodes can be of various types including needles, discs, or adhesive electrodes. An electrode pair consisting of a cathode and anode is secured over the nerve. The resistance between the electrodes and the skin should be <5 kΩ to ensure adequate stimulus delivery and avoid large stimulation artifact. Needle electrodes provide a low resistance and avoid resistance changes over long cases. For disc or adhesive electrodes, skin preparation with an abrasive is used to reduce electrical impedances. Patients allergic to citrus fruit may have a reaction to the skin preparation gel containing lemon. If using an electrode paste, it should be free of calcium to avoid chemical burns from iontophoresis into the skin.

Rate

The repetition rate must strike a balance between rapid data collection and recording of a quality waveform. Typical repetition rates are between 2 and 5 stimulations per second. A complete data set can usually be obtained within a couple of minutes at these rates. Repetition rates >5 per second sacrifice data quality for more rapid collection. The amplitude of the peaks will decrease appreciably as rates are increased above 5 pulses per second due to refractory times of the individual nerve fibers. Stimulation rates should avoid exact multiples of 60 Hz (or 50 Hz) to avoid line noise artifact.

Recording

Recording bioelectric signals involves optimization of several factors. At the beginning of a case, the best potentials should be optimized and set as baseline recordings suitable for comparing subsequent data with during the procedure. Quality baseline recordings are essential to providing the surgeon with accurate data interpretation. Scouting for optimal baselines includes evaluating different recording sites, filter settings, and other parameters. A simple one-size-fits-all approach to SEP monitoring often leads to a suboptimal recordings. The expertise of the monitoring team is in establishing the best recordings for each patient.

Recording Sites: General Comments

SEP recordings are made from different points along the DCML pathway. These points are chosen to provide recordings from peripheral, subcortical, and cortical potentials. In general, the active electrode is placed as near as possible to the anatomic generator, and a reference electrode is placed some distance away. The reference may be another scalp site or a non-cephalic site. Bipolar recording montages compare inputs between two nearby electrodes, while referential recording montages compare inputs between an active electrode near the anatomic generator and a much further placed reference electrode. The amount of electrical noise is proportional to the distance between the active and recording electrode as well as the distance between the anatomic generator and the active electrode. While the cervical potential is more susceptible to electrical noise because of the distance of the generator, these potentials are less affected by inhalation anesthetic concentrations (due to the lack of synapses up to this point in the pathway). For this reason they often are included in the recording montage despite their predisposition to noise.

The surgical field may make first choice recording sites inaccessible. When this happens, it is necessary to scout for alternate recording sites that will yield the highest possible recordings. Neurosurgical craniotomies may displace scalp sites. Cervical surgery may displace cervical recording sites. Several nearby alternate sites may be tried.

Site Nomenclature

The International Federation of Clinical Neurophysiology's 10–20 System provides the accepted naming convention for scalp recording sites. The 10 % extension of the 10–20 system [1] adds additional nomenclature. The EEG chapter in this book has further information on electrode nomenclature. For those unfamiliar with the naming conventions, a brief overview is given here. Electrode sites are named in a coordinate fashion with the first part of the binomial indicating the position along the anteroposterior axis and the second part of the name indicating mediolateral position. A series of anteroposterior lines are named according to their position relative to certain brain features. The C-line runs generally along the central sulcus. The P-line is at the level of the parietal lobe. The line in between the C-line and P-line is the CP-line. Mediolateral positioning is named relative to the lateral distance from the Z-line which runs along the vertex of the skull (midline). Odd numbers are to the left of the Z-line and even numbers to the right. The smaller the number, the closer to the Z-line. For example, an electrode placed over the right postcentral

gyrus near the hand area (lateral) would be CP4. The midline position would be named CPz. The location halfway between CPz and CP3 is known as C1. The letters "*i*" or "*c*" can replace the numbers when referring to general positions as either ipsilateral or contralateral, respectively.

Estimating recording sites by visual gross inspection frequently instead of measuring locations according to the 10–20 system misplaces electrodes by a centimeter or two and may result in suboptimal recordings and poor ability to reproduce recordings if an electrode needs to be replaced after falling off.

SEP IOM also uses non-cephalic recording sites, e.g., over vertebral spines and at Erb's point. Erb's point is located above the clavicle, 2 cm lateral to the insertion of the sternocleidomastoid muscle. Sites over vertebrae are referred to with their spinal level, sometimes including the term Sp for *spine*. In that way, CSp5 is located over the fifth cervical spine's posterior spinous process.

Some recommended technical parameters given in Table 6.1.

Lower Extremity SEP Recording Channels

Lower extremity SEP recordings are made from CSp5 and the scalp. The CSp5 channel monitors the cervical-brain stem activity, and the scalp channels monitor cortically generated peaks.

There is no one correct scalp recording site for the cortically generated peak of the lower extremity SEP. The dipole of the generator is oriented differently in different patients and can change with depth of anesthesia. Principal sites for the active electrode include CPz, CP1, CP2, CP3, CP4, and CPz. The orientation of the neurons that generate the potential changes as the postcentral gyrus bends toward midline. The orientation of the midline neurons that generate the cortical potential in response to lower extremity stimulation causes the dipole to project across the midline. This dipole projection results in a "paradoxical localization" of the potential over the scalp ipsilateral to the site of stimulation. This is paradoxical in that the neurons generating the potential are located in the contralateral hemisphere (as indicated by DCML pathway anatomy). Common sites for the active electrode are CPi, CPc, and CPz.

Choosing a site for the reference electrode is no less important. Scouting among possible recording channels early in the case helps to find the best channels to monitor that patient, although time may not permit this exercise. References may include the forehead, ear, mastoid, or the scalp location contralateral to the active electrode. Short distances between the active and reference electrodes (e.g., CPi–CPc) reduce noise but also may reduce peak amplitudes.

The subcortical peaks may be recorded over the spinous process of C5 (CSp5) with an ear, forehead, or shoulder reference. The subcortical peaks are less affected by anesthesia due to the lack of synapses at this point of the DCML pathway. Peripheral recording sites include the popliteal fossa or over the lumbar and thoracic vertebrae such as TSp12 or LSp1. Older or obese patients may have no recordable lumbar potentials as a normal variant.

Upper Extremity SEP Recording Channels

For upper extremity SEPs, recordings are made at the shoulder, cervical spine, and scalp. Scalp sites are generally optimum over the contralateral postcentral gyrus (CPc) with a forehead, ear, or mastoid reference. Subcortical peaks are popularly recorded from CSp5, earlobe, or mastoid with a reference located either at the forehead or contralateral Erb's point. An Erb's point channel (referenced to the contralateral Erb's point) can be used to test peripheral conduction and is useful for monitoring changes secondary to positional issues.

Filters

The typical low-frequency filter is set to 30 Hz and high-frequency filter 1,500–3,000 Hz. This balances control over noise while maintaining

most SEP peak characteristics. These settings reduce random amplitude fluctuations and some anesthetic-related variability [2]. Properly set filters will yield reproducible SEPs with minimum background variability in amplitude and latency.

Notch filters should not be used during SEP recording. The notch filter can cause a stimulus artifact with a decaying sinusoidal tail with peaks at 16.6, 33.3, and 50 ms. Those peaks easily can be mistaken for stable EPs at 16.6 or at 33.3 ms. This is called ringing artifact.

Digital smoothing filters are available on some equipment. They can distort the peak, possibly mixing artifact with a peak in ways that make interpretation more difficult.

It is always recommended to eliminate the cause of the noise when possible instead of masking it and to scout to find channels that are less affected by noise. Sometimes changes can be made to filter settings, but with care to avoid the negative effects of such changes. These effects include changing the signal morphology as well as introducing a phase shift.

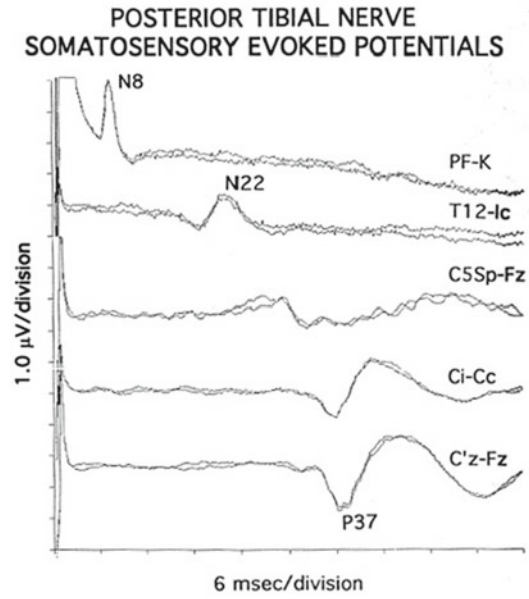

Fig. 6.2 Somatosensory-evoked potentials from posterior tibial nerve stimulation are shown. Typical peaks N8, N22, and P37 are noted. A cervical peak was also found. These peaks have normal latencies and amplitudes. *PK* popliteal fossa, *K* knee, *T12* T12 spine, *Ic* contralateral iliac crest, *C5Sp* C5 spine (From [3], with permission)

Primary Peaks

Lower Extremity SEPs

The P37 is the primary cortical peak generated by the somatosensory cortex. Often it is seen on the scalp ipsilateral to the leg stimulated at 37–45 ms after PTN stimulation at the ankle in normal patients, longer in taller individuals, the elderly, or those with pathology. The generator of the P37 lies in the vascular territory of the anterior cerebral artery. Figure 6.2 shows the lower extremity SEP peaks and nomenclature in a typical case.

The cervical peak is a far-field signal seen around 31 ms after stimulating the PTN at the ankle. The likely generator of this (N31) peak is the nucleus gracilis at the cervicomedullary junction. A trough following the cervical peak may represent conduction along the medial lemniscus or a thalamic potential. Amplitude and latency measurements for the cervical peaks are used especially when the cortical P37 is poorly suited for monitoring. Anesthetic has much less effect on the cervical peaks due to the presence of fewer synapses, so the cervical peak is more stable when anesthesia effects are prominent. These subcortical potentials lie in the vascular territory of the vertebra-basilar complex.

The N22 peak is a negative potential around the T12 spine occurring approximately 22 ms after stimulation. It is generated in the lumbar spinal cord, i.e., anatomically around the T12 spine. It represents the culmination of peripheral pathway conduction all the way up to and into the lumbar spinal cord. Peripheral peaks are monitored to clarify that decreased cortical potentials are due to a surgical problem rather than a problem with the stimulus or a positional issue. The popliteal N8 peak also could be used in a similar way.

Upper Extremity Peaks

The N20 is the cortically generated peak for upper extremity SEP IOM. The peak's amplitude and latency are measured and used as criteria to monitor neurologic function. The peak arises

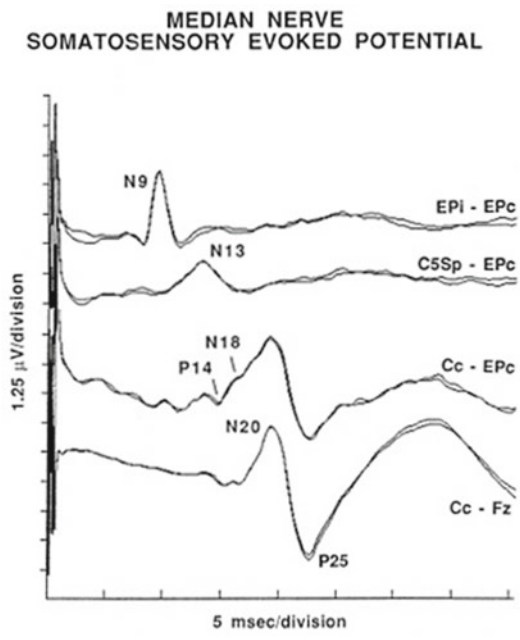

Fig. 6.3 Somatosensory-evoked potentials from median nerve stimulation are shown. Typical peaks are shown in each of four recording channels. The test is normal. *EPi, EPc* Erb's point ipsilateral, contralateral (From Nuwer et al. 1994, with permission)

from the primary somatosensory cortex (contralateral to the side of stimulation) on the postcentral gyrus. It is best seen recorded from an active electrode at CPc. The N20 lies in the vascular territory of the middle cerebral artery.

The subcortical peak is recorded with the same montage used for recording lower extremity subcortical potentials. The cervical spinal cord or possibly the nucleus cuneatus generates a negative peak approximately 13 ms following stimulation of the median or ulnar nerve. This N13 peak is followed by a positive (P14) peak generated by the medial lemniscus and an N18 from the thalamus. The N18 is often obscured by its proximity to the N20. For this reason, a CPi–EPc recording channel is used to isolate the N18. These subcortical potentials are in the vascular territory of the vertebra-basilar complex.

A peripheral N8 peak is recorded over the brachial plexus at Erb's point. The blood supply for this potential is the axillary artery. Figure 6.3 illustrates typical upper extremity SEP peaks and their nomenclature.

Interpreting Change

Characteristics of the SEP waveform including latency, amplitude, and area under the curve are useful in interpreting changes from baseline. In order for any test to be useful for the purposes of IOM, it should have an adequately high sensitivity and specificity. When changes in latency and amplitude are used for SEP IOM, this test is nearly 100 % sensitive and specific. This means that there are very few false positives or negatives with SEP monitoring. Alarm criteria for SEP IOM is a 50 % decrease in amplitude and/or a 10 % increase in latency [3, 5]. When these thresholds are crossed, the monitoring team quickly assesses the reason for the change. Technical issues should be quickly resolved. Changes due to anesthesia should be documented and communicated with the surgical team and anesthesiologist. Surgical-induced changes should be immediately reported to the surgeon as they may warrant intervention.

Anesthetic effects are one of the main reasons for an SEP IOM change. Volatile inhalants, nitrous oxide, or bolus injections may reduce the amplitude of the SEP signal. Since anesthetic works primarily at synapses, cortical potentials are most susceptible to anesthetic effects, while subcortical and peripheral potentials remain relatively stable. *Anesthetic fade* refers to a gradual reduction in amplitudes during the first 30 min after induction and to a smaller extent over subsequent hours of a long case. Anesthetic fade is most common with inhalation anesthetics.

Preexisting impairment may magnify anesthesia effects (Fig. 6.4).

Technical problems should be ruled out when signals change. When a technical issue is suspected, it is important to distinguish between a stimulation and recording issue. Large increases in electrode impedance suggest a recording issue such as a dislodged electrode. Absence of a stimulation artifact or poor current return indicates that there is a problem with stimulus delivery. Another common recording issue is the introduction of electrical noise. In this case, the live (unaveraged) waveform should be viewed and the frequency band of the noise be identified. The first priority should be to find and eliminate the source of the

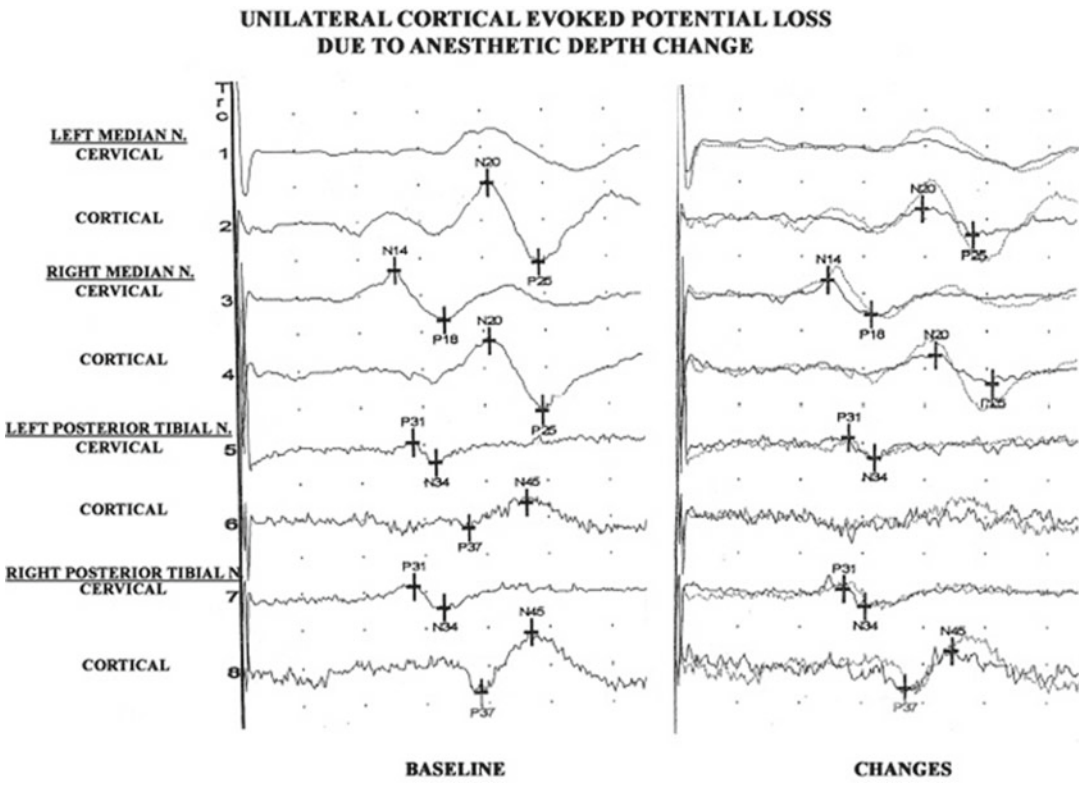

Fig. 6.4 The baseline testing shows a relatively attenuated left lower extremity cortical peak (*left* tracings). After an increase in anesthetic depth (*right* tracings), that channel no longer shows a reliable SEP (The baseline is superimposed on the newly acquired tracings at the *right*.) An anesthetic effect is the likely cause of the change, as suggested by both the preserved subcortical peaks for the affected pathway and somewhat attenuated cortical peaks in all other pathways (From UCLA Dept. Clinical Neurophysiology, with permission)

noise. If that fails, changing the pass band by adjusting filter settings may be required.

Perisurgical factors may also induce SEP data changes including hypothermia, hypotension, and hypoxia. Cooling can increase latencies. Cooling can be systemic, in a limb, or because of local irrigation. Substantial cooling can cause SEP cortical peak amplitude loss, even decreased to isoelectric recordings at temperatures below 22 °C (Fig. 6.5). Preexisting spinal cord compression may leave a patient especially sensitive to hypotension due to autonomic dystonia. Correlation of SEP changes with the anesthesia doses, the patient's temperature, and blood pressure will help determine the cause of change and a solution. It should be mentioned that just because a change is not deemed surgical does not make it clinically insignificant. A change resulting from hypotension indicates that the brain is not being adequately perfused. It is necessary to communicate this to the surgeon and anesthesiologist so that corrective action may be taken.

Surgical problems also cause changes, which is likely the reason you were asked to monitor the case to begin with. Types of surgical issues that can cause data changes include direct blunt trauma, excessive retraction or compression, stretching of structures, vascular insufficiency, vasospasm, embolus, thrombus, or other clinical problems. Not all decreases in amplitude are clinically significant, meaning not all will result in a

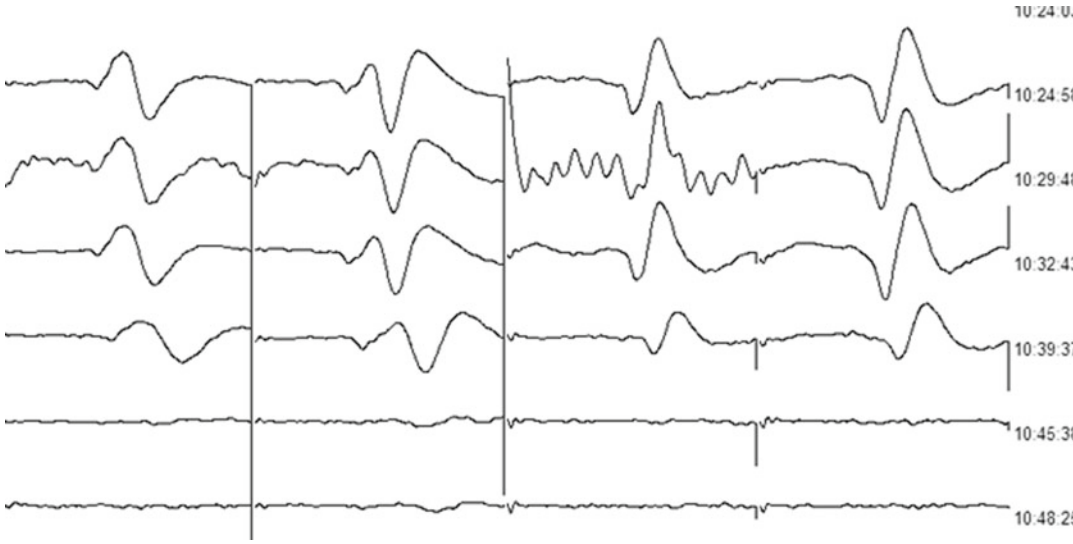

Fig. 6.5 Temperature effects on SEPs. Left and right median and left and right posterior tibial nerve SEPs are shown over 25 min as the patient's core temperature dropped from 34 to 20 °C. Time flows from top to bottom. Latencies increase, amplitudes decrease, and then the peak essentially disappears

deficit. The chances of an amplitude reduction resulting in a negative outcome increase as the amplitude approaches and passes 50 % of baseline and increases the longer the change persists. Early identification of changes leading to prompt intervention is critical to preserving function. A 50–80 % transient amplitude decrease for only a few minutes poses a small-to-modest risk of postoperative neurologic deficits, especially if the SEPs return promptly to baseline values following intervention. Higher risk is incurred with abrupt changes, complete loss, and persistent attenuation. The gravest situation is the abrupt, persistent, complete loss of previously easily detected SEPs. Even an abrupt persistent loss does not always predict impairment. The risk in that case is about 50–75 % [5]—a deficit is not a foregone conclusion.

Stable intraoperative SEPs are highly predictive of a good neurological outcome. A patient will have a neurologic injury despite the preservation of intraoperative SEPs in fewer than 0.1 % of cases (Table 6.2). This degree of sensitivity and specificity makes SEPs the gold standard for intraoperative spinal cord monitoring. IOM-prompted surgical interventions are successful at reducing postoperative neurological deficits. The use of IOM reduces paraplegia by 60 % for spinal surgery [5].

Finding the Motor Cortex

In addition to monitoring, SEPs can be used to test for the location of motor cortex. The median nerve SEP stimulation technique is used. Recording is from a 1 by 8 strip of cortical electrodes laid directly onto the exposed cerebral cortex. A nearby reference electrode is placed at a neutral site such as on dura or muscle. The N20 peak appears at the primary somatosensory cortex on the posterior edge of the central fissure. By determining the location of the N20, one can deduce that the next more anterior gyrus is the motor cortex. The strip may need to be moved several times to find the thumb level of sensory cortex that corresponds to the median nerve stimulation site.

Clinical Indications

There are many indications for the use of SEPs in the operating room [6]. The most common use is for spinal cord monitoring in cases involving scoliosis, cervical myelopathy, fractures, tumors, and other disorders that put the spinal cord at risk during surgery. SEPs also are used to monitor the intracranial portions of the somatosensory pathways. For example, SEPs are useful for monitor-

Table 6.2 Neurologic outcome prediction rates for SEP monitoring in spinal surgery

False-negative rate	
Neurologic postoperative deficits despite stable SEPs	
Definite	0.06 %
Total	0.13 %
False-positive rate	
No neurologic deficits despite SEP changes	
Definite	0.98 %
Total	1.51 %
True-positive rate	
Neurologic deficits predicted by SEP changes	
Definite	0.29 %
Total	0.42 %
Neurologic deficits	
False negative plus true positive	
Definite	0.36 %
Total	0.55 %
Sensitivity	92 %
Specificity	98.9 %
Positive predictive value	42 %
Negative predictive value	99.93 %

These data are from a large multicenter US outcome study of SEP spinal cord monitoring organized through the Scoliosis Research Society. Note the rate of definite false-negative cases is low (0.06 %). The very high negative predictive value here indicates the high reliability of the monitoring when the SEP remains normal and stable. The outcome survey report [4] discusses in detail these data and related assumptions

ing the brain stem during surgeries to remove cerebellopontine angle tumors, during cranial nerve microvascular decompression procedures, brain stem and cerebellar tumor resections, aneurysm clippings or coilings, and decompression of Chiari malformations. SEPs are used to monitor the internal capsule and cerebral cortex for ischemia during carotid endarterectomy, brain tumor removal, arterial-venous malformation resection, aneurysm clipping, epilepsy surgery, and other procedures placing the cerebral cortex at risk.

In each case, similar SEP parameters and criteria for change are used. The nerve chosen for stimulation may differ based on the objective of the procedure. Median and posterior tibial nerve SEPs are monitored most often. The peroneal nerve at the knee may be substituted for the posterior tibial if the patient has a peripheral neuropathy or has an amputation below the knee. The ulnar nerve is used in place of the median in spine surgery at or below C6 to give better coverage of the whole cervical spine. The ulnar nerve is also most vulnerable to positional injury, so monitoring the ulnar nerve SEPs during thoracic or lumbar cases is indicated.

For intracranial cases, the choice of SEP monitoring should depend on the vascular territory at risk. Lower extremity SEPs are important to monitor for cases involving risk to the vascular territory of the anterior cerebral artery. Upper SSEPs monitor the territory of the middle cerebral artery. For any intracranial case, the recording electrodes may need to be moved because of the craniotomy flap. Figure 6.6 shows an example of an SEP recorded from alternate scalp locations during an aneurysm clipping.

If SEP IOM is being used to protect a peripheral nerve such as the sciatic, then the anatomy will dictate the proper stimulation sites. For example, when monitoring sciatic nerve, you should be aware that the peroneal and posterior tibial portions travel side by side, with the peroneal portion that is most at risk during hip replacement surgery. In case in which the sciatic nerve is at risk, it may be appropriate to monitor both the posterior tibial and peroneal nerves.

SEP IOM remains the modality best supported in the literature. In a formal assessment process, the American Academy of Neurology and the American Clinical Neurophysiology Society jointly concluded and recommended that IOM is established as an effective means to predict an increased risk of the adverse outcomes of paraparesis, paraplegia, and quadriplegia in spinal surgery based upon four Class I and seven Class II studies. Surgeons and other members of the operating team should be alerted to the increased risk of severe adverse neurologic outcomes in patients with important IOM changes [7]. A large multicenter study of spinal cord SEP monitoring showed a 60 % decrease in paraplegia and paraparesis associated with monitoring [5]. Validity measures and neurologic deficit rates from that study are shown in Table 6.2.

Sala et al. [8] studied motor outcomes for intramedullary spinal cord tumor surgery. Historical controls were used from the time prior to adoption of IOM. If IOM showed changes, myelotomy was moved to a different location along the tumor or temporarily stopped. Sala

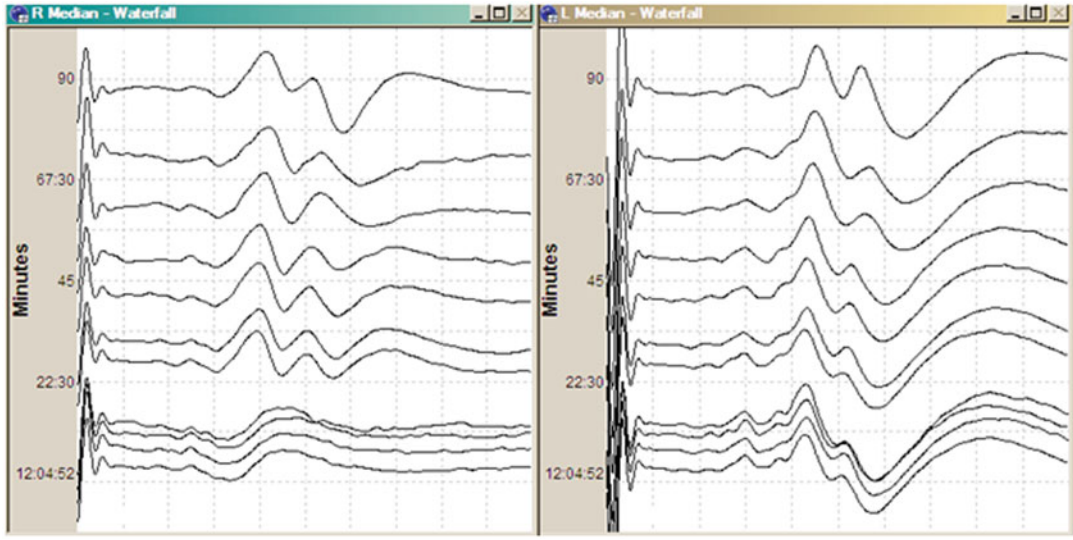

Fig. 6.6 A 68-year-old woman during left internal carotid artery aneurysm clipping after a subarachnoid hemorrhage complicated by arterial dissection. During surgery, the right median (shown) and posterior tibial (not shown) SEPs cortical peaks for the left hemisphere were lost within 20 min of clipping, at a time when further aneurysmal bleeding was encountered. Time reads from the top downward (later tracings at the *bottom*). Ninety minutes of the monitoring is shown around the time of clipping. Note how the N20 peak is replaced by a lower amplitude far-field potential generated at the thalamic or high brain stem level, so the tracing is not flat. At the same time, the contralateral side remains stable. This patient suffered a thrombosis in the middle cerebral artery territory ischemic infarct despite the SEP alarm

measured McCormick grade of weakness for patients with EP monitoring compared to patients without EP monitoring. For the patients with IOM, the preoperative to postoperative change in McCormick grade of weakness was +0.28. For the patients without IOM, the preoperative to postoperative change was −0.16. The difference between groups was significant ($p < 0.002$).

A variety of animal studies also support the validity of IOM in raising an alarm at a suitable point in time that gives the surgeon enough time to intervene and avert a postoperative neurological deficit in many patients. For that reason, IOM SEP is considered clinically useful by most and should be used when there is reasonable risk of neurological injury from surgery.

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Questions and Answers

Questions

1. The best trade for SEP stimulation rate is often around
   (a) 3 per second
   (b) 5 per second
   (c) 7 per second
   (d) 9 per second
2. When cortical SEPs are low in amplitude, tactics to improve the signals include
   (a) Faster stimulation rates
   (b) Lowering the low filter setting
   (c) A smaller sample size to produce EPs more quickly
   (d) Turning on the notch filter
3. In the 10–10 system, electrode site CP2 is located
   (a) Halfway between Cz and P4
   (b) Halfway between Cz and C4
   (c) Halfway between Pz and P4
   (d) Halfway between C4 and P4
4. The peripheral recording site Erb's point is at
   (a) 5 cm above the mid-clavicle just lateral to the sternocleidomastoid
   (b) 2 cm above the mid-clavicle just lateral to the sternocleidomastoid
   (c) Above the clavicle 2 cm lateral to the insertion of the sternocleidomastoid
   (d) Above the clavicle 5 cm lateral to the insertion of the sternocleidomastoid
5. The most likely location to find the P37 peak for right posterior tibial SEP testing is
   (a) C1'
   (b) C2'
   (c) Cz'
   (d) CPz
6. Recording site PF is at
   (a) Posterior frontal
   (b) Popliteal fossa
   (c) Parietofrontal
   (d) Parafrontal
7. Criteria for change in posterior tibial SEPs commonly are
   (a) 10 % amplitude loss or 2 ms latency increase
   (b) 30 % amplitude loss or 3 ms latency increase
   (c) 50 % amplitude loss or 4 ms latency increase
   (d) 70 % amplitude loss or 6 ms latency increase
8. The greatest amplitude decreases in cortical SEPs are commonly associated with
   (a) Too high a setting of the stimulus intensity
   (b) Cooling to 32 °C
   (c) MAC use of inhalation anesthetics
   (d) Too low of a low filter setting

Answers

1. (b) 2. (b) 3. (a) 4. (c) 5. (b) 6. (b) 7. (c) 8. (c)

Motor Evoked Potentials

7

Jay L. Shils and Vedran Deletis

Introduction

Iatrogenic injuries are an undesired consequence of surgery, yet iatrogenic injuries to the motor system are much more devastating to a patient's quality of life than most injuries to the sensory system. Generally an injury to the spinal cord will be most likely be picked up by somatosensory evoked potentials (SSEPs), yet a focal injury to the anterior spinal artery (ASA) may be missed [1]. There is a lot of evidence in the literature describing selective injury to the anterolateral columns sparing dorsal columns with preserved SSEPs [2–5]. The inclusions of motor evoked potentials (MEPs) to the intraoperative monitoring *toolbox* can help to confirm/prevent selective lesions to the anterolateral columns of the spinal cord. Yet MEPs are not without their limitations. Even with these limitations, proper application and interpretation of MEP data can be a significant adjunct in reducing iatrogenic injury during surgery.

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History

Artificial stimulation of the motor system dates to 1664 when Swammerdam removed the heart of a frog and demonstrated that by gently stroking the severed nerve ends of the open wound the muscles would contract [6]. The most well-known experiment comes from Luigi Galvani when in 1771 he observed that electrical sparks applied to the nerves in the leg of a frog would cause twitches in the leg muscles [7]. In the 1860s Hitzig and Fritsch stimulated the exposed brains of soldiers using direct cortical stimulation (DCS) and found that they could cause *crude* movements [8]. They continued their work on live dogs and found that not only could they cause these *crude* movements, they also observed that specific areas, when stimulated, caused specific movements [9]. In the late 1930s, the neurosurgeon Wilder Penfield published his mapping studies of the human brain performed during epilepsy and tumor resection surgeries [10]. Penfield not only localized the motor and sensory areas of the brain but also defined the cortical somatotopy or motor and sensory homunculi of these two cortical areas. Penfield's basic stimulation technique, 60 Hz trains of stimuli lasting for one to a few seconds, is still practiced for cortical mapping of language and sensory areas (and in most neurosurgical centers, it is still in use for the mapping of motor cortex or subcortical pathways). In the 1950s Patton and Amassian were the first to record direct traveling waves from corticospinal tracts (CTs) when stimulating the motor cortex/subcortex in both

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cats and primates [11]. They observed two types of waves, the first was a short-latency triphasic response termed the D wave (direct wave) they interpret as a result of the direct activation of the CS tract and the second set of waves were termed I waves (indirect waves) interpreted as trans-synaptic activation of motor neurons of the CT within the motor cortex [12].

Research on the motor system continued, yet there existed no direct method to deliver stimuli to a subject's brain without accessing the brain directly given the extremely high impedance of the skull. In order to electrically cross this high impedance barrier, high stimulus currents are needed to activate the underlying neural tissue. In 1980 Merton and Morton developed a high-voltage single-pulse technique for the delivery of transcranial electrical stimulation (TES) to the intact human subject [13] (it should be noted that they discuss that this stimulation was "without undue discomfort" to the subjects).

One interesting study using this method was published after the work of Merton and Morton, by Levy et al., that delivered TES via an anodal electrode placed over the motor cortex and a cathodal electrode placed on the hard palate to record D waves, via either electrodes placed over the thoracic spinal canal or by inserting electrodes into the level of the bony laminae or directly in the epidural space during surgery [14]. They claimed that these recordings represented descending activity of the motor system. In addition to demonstrating the recording, Levy et al. discuss using multiple pulses to help produce motor activation at lower stimulation levels, yet this idea was not pursued [14] until much later as will be seen below. In the late 1980s Katayama and Tsubokawa recorded D waves from the epidural space of the spinal cord stimulating surgically exposed motor cortex [15]. Epidural spinal electrodes were inserted percutaneously into the upper thoracic epidural space under X-ray control and pushed cranially to the lower cervical epidural space. During surgery the motor cortex and other cortical areas were then directly stimulated using both monopolar and bipolar stimulation. They demonstrated that direct application of monopolar anodal current to the motor cortex required lower stimulation intensities as compared to monopolar cathodal bipolar stimulation [15]. In order to better refine the most optimal stimulation configuration and also to understand the phenomena of latency changes with increasing stimulation current, Burke et al. proposed the discrete jumps in latency to be due to bends in the CT as the stimulation moved deeper in the brain [16]. A set of papers by Deletis, Rodi, and Amassian described the neurophysiologic mechanism underlying MEPs in anesthetized humans which is of importance in understanding the pitfalls during the routine use of MEP monitoring in the operating room [17, 18].

Physiological Background for Monitoring the Motor System

Depending on the type, location, and intensity of stimulation, the MEPs recorded during intraoperative neuromonitoring (IONM) are generated and transmitted from a limited subset of neural elements. These responses are, for the most part, transmitted by the largest fibers of the CT, and in deeply anesthetized patients an artificial stimulus activates these largest fibers directly. The exception is in the awake subjects/patients or use of transcranial magnetic stimulation (TMS) where the pyramidal cell body is activated by interneurons ending up on the pyramidal cells in the cortical gray matter. Yet even given that we are testing a limited subset of the motor system, the data obtained with this method can still be useful for patient protection, and the physiology behind these responses needs to be properly understood in order to make proper data interpretations in the operating room.

Anatomy and Physiology of the Motor System

The motor system is a complex combination of neural subsystems existing in both the central and peripheral parts of the nervous system. It is important to realize that artificial stimulation most likely activates many different cortical fibers, while MEP monitoring techniques only

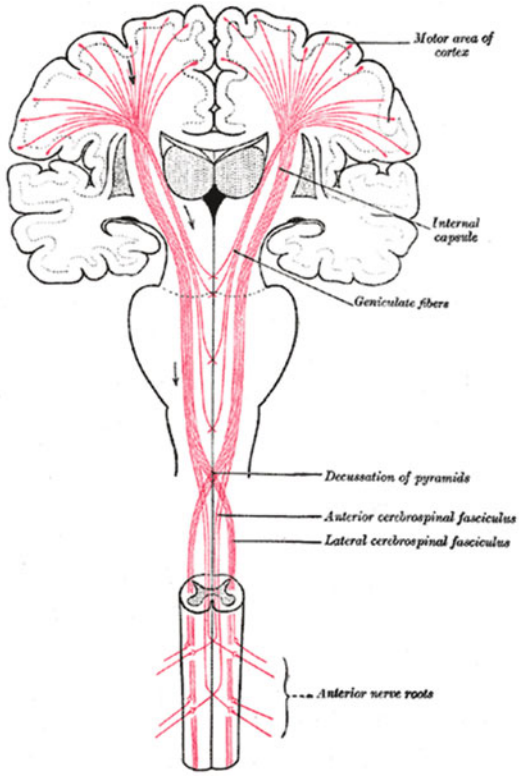

Fig. 7.1 Multiple areas of the cortex are involved in motor movements. In addition to the cortex, there also exist multiple subcortical areas. During artificial simulation under anesthetics, the corticospinal fibers are the main carriers of that stimulation information to the alpha motor neurons in the spine. Even though the stimulation will activate fibers from other areas, this information is usually not passed due to the synaptic junctions between the other areas and the corticospinal tract which under anesthesia are shut down for the most part (from http://thebrain.mcgill.ca/flash/a/a_06/a_06_cr/a_06_cr_mou/a_06_cr_mou.html (copy left) and with permission from the GNU free documentation license)

record responses from a small portion of them (Fig. 7.1). The primary anatomic structure of the MEPs is the Betz cell in layer five of the motor cortex and its axons in the CT and corticobulbar tract (CBT) (upper motor neuron), the spinal or α-motor neuron (αMN) and its axon (lower motor neuron), and the end organ (muscle). There also exist indirect corticofugal motor pathways not projecting directly to the spinal cord, but indirectly having interruption on their descending route to the αMN. The primary motor cortex, where the CT fibers originate, is located in the precentral gyrus and is primarily responsible for fine voluntary movement. This area of the cortex receives information from multiple cortical areas which include the extrapyramidal system (areas such as the basal ganglia and cerebellum) and sensory areas including somatosensory, visual, auditory, both parietal, and frontal cortices. The primary motor cortex has a map of the body, or homunculus, with the head located laterally on the cortex and the leg located within the interhemispheric fissure. The primary pathways that we are concerned with when monitoring MEP during surgery are depicted in Fig. 7.2.

At the surface of the cortex are six layers of gray matter. Each functional area of the brain has different proportions of each of these six layers, yet the basic six-layer structure is the same throughout the cortex. Each area of the cortex is defined based on its specific cytoarchitecture and neural organization. The nomenclature used for this differentiation is known as a Brodmann area [19]. Interestingly each Brodmann area generally corresponds to a specific functional area, even though the original differentiation was purely based on its cytoarchitecture (http://www.fmri-consulting.com/brodmann/Introduction.html). Generally layer 5 is the output while layer 4 is the input layer. The primary motor area (PMA), or Brodmann area 4, is located in the posterior portion of the frontal lobe just anterior to the central sulcus (Fig. 7.3). Layer 5 of the primary motor cortex contains large pyramidal cells known as Betz cells that send long axons directly to motor neurons located in the spinal cord or brainstem via the CS or CBT (the combination of these two tracts is known as the pyramidal tract). About 60 % of the human CT arises from the primary motor cortex and area 6 (premotor area and supplementary motor area); the other 40 % arises from the somatosensory cortex (areas 1, 2, and 3) and cingulate cortex (areas 23 and 24) [20, 21]. Even though all areas of the body are represented within the primary motor cortex, it appears that more proximal and axial muscle fibers in the CT have their origins in the premotor area (area 6), while the distal musculature tends to have its origin in the PMAs (area 4) [22]. Since both sets of

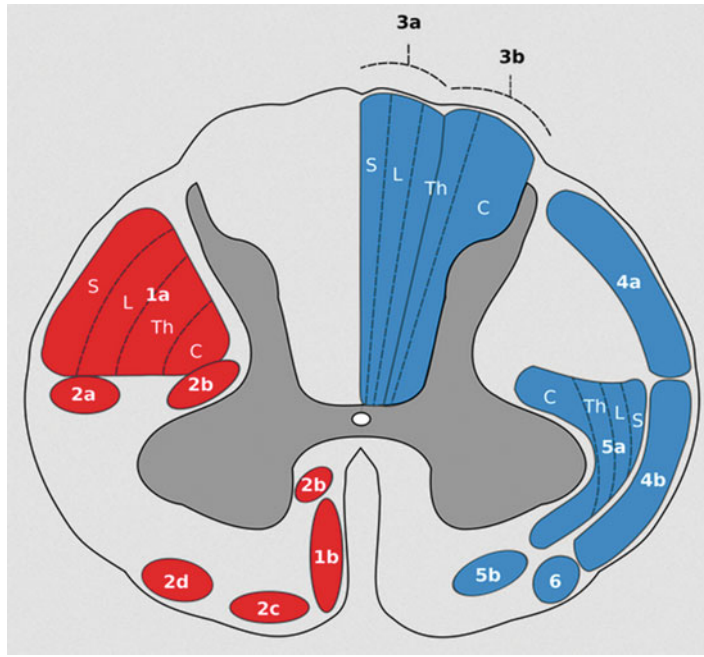

Fig. 7.2 The corticospinal and corticobulbar pathways. The pyramidal fibers originate in the motor cortex and traverse through the internal capsule. At this point the corticobulbar fibers are medial and synapse on the secondary axons in the brainstem. Most corticospinal fibers decussate in the medulla and travel in the lateral corticospinal columns to synapse at the alpha motor neurons located in the anterior horn of the spinal gray matter. The lateral corticospinal tract (1a in the figure) shows a lateral to medial homunculus with the sacral region being most lateral and the cervical region being most medial. Region 1b is the anterior corticospinal tract in the spinal cord (2a from Gray's anatomy. 2b with permission from Wikimedia Commons)

fibers are contained in the CT, stimulation used during IOM will activate both of them. From the cortex the CT funnels into the anterior half of the posterior limb of the internal capsule and then travels between the thalamus and parts of the basal ganglia (striatum and globus pallidus) to the ventral portion of the cerebral peduncles (in the middle two fifths of the cerebral crus—anterior portion of the cerebral peduncles). At this level the fibers that will eventually synapse on αMNs in the spinal cord gray matter innervate leg muscles and are lateral to fibers eventually innervating hand muscles. From the midbrain the CT fibers enter the pons and pass through the pontine nuclei where fibers going to the leg muscles are now located ventrolateral relative to the fibers going to the hand muscles. The CT enters the ventral part of the medulla forming part of the medullary pyramids where fibers innervating the lower limbs are located ventrolateral compared to the fibers innervating the upper limbs. At the lower level of the medulla, 80–90 % of the CT decussates with most fibers entering lateral CT of the spinal cord. Fibers going to the lower limb muscles tend to cross more rostrally than for the upper limbs. The 10–20 % of uncrossed fibers in the anterior CT innervate αMN ending on more proximal and trunk musculature [23].

There are about one million fibers in each CT with around 2 % of these fibers being large 11–20 μm which are known as fast conducting corticospinal fibers (conduction around 50 m/s). CT fibers for the upper limb are more medial than lower limb fibers. The rest of the CT fibers synapse on other interneurons within the gray matter of the spinal cord. The large CT fibers are essential for eliciting MEPs. About 55 % of all CT fibers end in the cervical region with 25 % innervating the lower limbs. The rest innervates the thoracic region. It is interesting to note that the

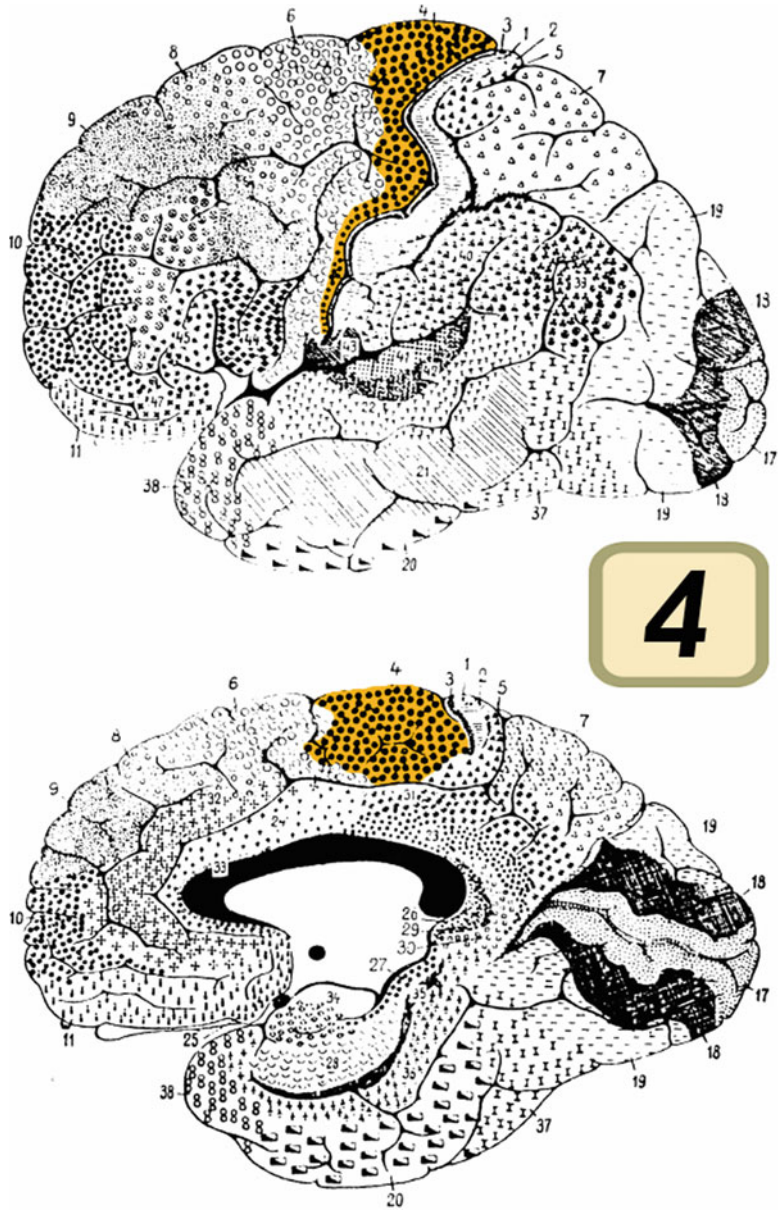

Fig. 7.3 Map of the cortex with all of Brodmann areas depicted. Area 4, the primary motor cortex, is *highlighted*. Area 4 is just anterior to the central sulcus (with permission from Wikimedia Commons—public domain)

CT is not symmetric, and it appears that CT fibers that cross more anterior tend to form the larger CT in the cord whether it is the right or the left [24]. A single αMN has over 1,000 synapses yet only around 22 dendrites [25]; thus in the awake animal generation of an action potential in the αMN is a complex process of competing systems. In the anesthetized animal this complex system is shut down due to anesthetics. In addition to αMN CT inputs, there are inputs from interneurons driven by other CT fibers, inhibitory interneurons, Renshaw cells (which are inhibitory), sensory Ia and Ib fibers, and other descending tracts including the rubrospinal tract, vestibulospinal

tract, reticulospinal tract, and tectospinal tract. Many of these presynaptic fibers synapse at many places on the αMN, instead of one point. Due to the large number of synapses, it appears that the control of the αMN is multifactorial. In the non-neurologically compromised awake human, all the synaptic inputs to a specific αMN modulate the membrane potential; thus appropriate supratentorial modulation appropriately depolarizes the cell.

The CT enters the gray matter of the spinal cord in the ventral horn and fans out terminating in laminae IV through IX. Yet the largest CS fibers appear to make monosynaptic connections to the αMN in laminae IX [26]. Most of the CT tends to synapse on interneurons, some of which being part of circuits that modulate the αMN, while others influence motor circuits such the γ-motor system. Axons from the αMN innervate muscle fibers of a single muscle. The αMN and its axon are known as the lower motor neurons. The combination of the αMN, the terminal branches of the αMN, and the muscle fibers they innervate is known as the motor unit. Each motor unit is innervated by one axon and thus only one αMN.

Damage to either the upper motor neurons or the lower motor neurons will cause paralysis. Damage to the lower motor neuron will result in what is known as a flaccid paralysis—no muscle tone and no movement. Damage to the upper motor neuron shows in a much more complex set of symptoms but generally includes no voluntary movement and a range of muscle tone from minimal tone to severe spasticity.

Indirect damage to the motor system can arise from reducing the blood supply to the critical structures. The cortex is supplied primarily by four main vessels, the two carotids and the two vertebral arteries. These four vessels supply the circle of Willis (COW) presenting connection between the carotid and vertebral arteries. The COW, with basilar artery complex, converts the flow from these four vessels into a network supply for the brain and brainstem. The middle cerebral artery (MCA) coming from the carotid artery supplies the lateral motor cortex and its descending axons. The anterior cerebral artery (ACA) supplies the medial parasagittal motor cortex and its descending axons originating from the motor cortex. Axons at the CT within the internal capsule are supplied by lenticulostriate branches originating from the MCA and the anterior choroidal arteries. At the level of the brainstem, the CT is supplied by branches of the vertebral and basilar arteries. The spinal cord is supplied by one ASA, two posterior spinal arteries (PSA), and a varying number of radicular arteries. The ASA supplies the anterior 2/3 of the spinal cord including the lateral and anterior CTs and the ventral horn. In the adults the ASA is formed via fusion of the anterior spinal branches of the vertebral arteries, while the PSA originates from the posterior inferior cerebellar arteries [27]. In the thoracic spinal cord, there is usually one large supply vessel coming from the aorta known as the artery of Adamkiewicz and two or three smaller vessels. Interestingly, in about 10 % of patients this vessel enters the spine at the L1–L2 level [28]. This variability in supply demonstrates one of the critical needs for neuromonitoring. Normally watershed zones are most commonly at levels T1, T5, and T8–T9 where reductions of blood flow in any of the feeder vessels can cause significant ischemia at these regions [27].

Electrophysiology

Artificial stimulation (both electric and magnetic), such as is used for intraoperative monitoring, may be applied at multiple levels of the nervous system, yet no matter where stimulation is applied, there are in general two primary types of recorded response in the anesthetized patient: (1) recording conducted volleys traveling along the spinal cord and (2) recorded compound muscle action potentials (CMAPs). The latter one records the muscle response activated from excitation of the αMN. In general stimulation is applied at the level of the motor cortex or subcortical part of the CT, the spinal cord, or peripheral nerve. Each of these areas requires different stimulation parameters that will be described in the next section.

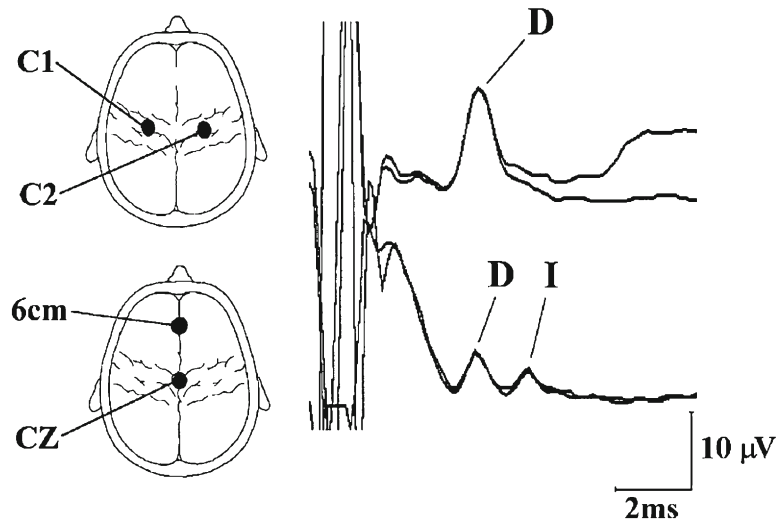

Fig. 7.4 Upper thoracic epidural recordings of D and I waves in a 14-year-old female during surgery for a low cervical intramedullary tumor. The upper trace was obtained after transcranial electrical stimulation over C1 (anode) and C2 (cathode) using 140 mA stimulus intensity and a stimulus duration of 500 **μ**s. The lower trace was obtained after anodic stimulation at Cz and cathodal stimulation at 6 cm anterior to Cz, using the same stimulus duration but at 200 mA. Note the appearance of the D and I waves with this electrode arrangement. (An upward deflection is negative.) Reprinted from [29]

The descending volleys along the CT, initiated via stimulation, originate from two separate but not independent circuits. The first response, defined as the D wave, (Fig. 7.4) or direct response, results from the direct stimulation of the CT fibers in the cortex. This response can come from either stimulating the axons directly or also stimulating the gray matter in turn generating the axonal response. The second set of responses is defined as I waves, or indirect waves (Fig. 7.4), resulting from local circuits in the cortex being activated by the stimulus. It has been shown that the amplitude of the D wave is proportional to the intensity of the stimulation of the subcortical white matter up to a certain point, which most likely represents the activation of the entire CT [30]. It was also observed that the latency did not increase linearly with an increase in stimulation intensity. Late in the 1980s Rattay demonstrated that the point of action potential initiation on an axon is most likely to occur at bends or curves [31]. These sudden *jumps* in latency correspond to the location of the CT bends at the level of the genu of the internal capsule and the level of the brainstem. This fact is important since if surgery is targeted at a specific area in the brain, you need to make sure that the stimulation does not directly activate CT fibers more caudal in the brain or brainstem from the point of surgical intervention.

Given that D waves result from a direct activation of the cell body or axon, and the fact that the response is recorded from the axon, these responses are unaffected by anesthetics. I waves on the other hand will usually not appear during IONM given that they are generated via circuit pathways and contain synapses blocked by anesthetics. For the most part recording descending volleys along the CT is an invasive procedure and is not used in most spinal and cranial procedures. It is the CMAP recording that is the result of the stimuli activating the αMN and in turn generating a CMAP. Given that the αMN is a highly modulated cell, the effects of anesthesia are important in understanding the behavior of the CMAP response. As anesthesia starts to shut down synaptic transmission, it becomes increasingly difficult for a single pulse on one CT fiber to be able to generate a CMAP (although in some cases high-intensity long pulse stimulus durations

will generate a CMAP). In order to compensate for the effect of anesthesia, it was found that a multi-pulse technique was necessary. It is important to remember that the multi-pulse technique is needed for generation of a CMAP, but the D wave can be generated with a single pulse. Although, it is interesting to note that when under anesthesia I waves are lost, thus giving credence to the synaptic nature of I waves. It should also be noted that the effects of I waves and the multiple tract inputs to the αMN are not necessarily the same as the artificial creation of a temporal train of D waves reaching the αMN at one input, even though the end result is the same [17]. When looking at the different anesthetic agents, it has been demonstrated that inhalational anesthetics are the most effective in abolishing the muscle MEP response [32–35]. It should also be noted that the blocking effects of inhalational anesthetics are not linear at the αMN; thus the ISI between train of stimuli will need to change as concentrations change [33, 34]. This study showed that for low to moderate doses of isoflurane and NO_2, an ISI between 3 and 6 ms was optimal for producing CMAPs, yet for high concentrations only 1 ms produced CMAP. Given that they studied using NO_2 alone and found no major difference between the concentration and ISI, they concluded that isoflurane was the primary culprit. At our institution we find that shorter ISIs help elicit MEPS when higher doses of inhalational agents are used and make less of a difference with a pure TIVA regime. A common technique is to use an opioid with propofol, which can cause some minor change in the amplitude of the MEP; the effect is much less pronounced than that caused by inhalational agents. Scheufler et al. investigated varying doses of propofol (combined with constant remifentanil infusion) with different ISI and stimulus intensities and found that an ISI of 1 ms produced the largest MEP response for a given dose of propofol [36]. It is important to note that in some cases, for patient safety, a specific anesthetic may be needed that is not optimally compatible when eliciting MEPs, and it is critical that the IOM technologist and neurophysiologist have a good line of communication with the anesthesiologist and surgeon.

The intraoperative technologist or neurophysiologist can also modify the stimulus to help minimize the effects of anesthesia. The multi-pulse technique usually consists of a train of 5–9 pulses with an interstimulus interval of 1–4 ms. Some groups [37] describe using a 500 μs pulse width, while some IONM equipment does not allow for stimulation pulse widths above 50 μS.[1] It is important to note that no definitive study has been performed investigating the optimal pulse width for MEPs which leaves the monitoring community divided between short 50 and 500 μs pulses. In practice, using a 50 μs pulse width requires higher intensities compared to the 500 μs (personal author observation JLS) pulse, yet the total charge delivered per phase (which is related to the likelihood of tissue damage) in the two cases has not been systematically studied in a large group of patients either. MacDonald [38], in a unpublished report, performed a theoretical analysis based on the limited existing data and calculated that the optimal ISI range is between 50 and 800 μs; thus both values safely fit in this range, just at opposite ends. In 1993 Taniguchi et al. studied the various stimulation parameters during craniotomies [39]. Using both cathodal and anodal monopolar stimulation, Taniguchi et al. looked at stimulation pulse width, train length, and ISI. In the Taniguchi study they found that an ISI of two ms was the optimal (i.e., minimal stimulation intensity to obtain a maximum MEP response) yet this varies with age, anesthetic regime, and functional integrity. Using these results some groups have demonstrated that when a nonoptimal MEP is obtained, one should try varying the ISI (Journee et al. personal communication). This is important since for the αMN to reach firing threshold, the temporal relationship between the D wave volleys is critical. When Deletis et al. investigated the relationship between D and I wave generation and the generation of CMAPs, they found that short trains with an ISI of 4 ms were optimal in eliciting responses in the tibialis anterior muscle (TA) due to a complete recovery of the D wave amplitude and even the generation of some I waves where an ISI of 2 ms required more stimuli [17]. This rule can be

[1] At the time of this writing.

applied when using moderate stimulation intensity. With high stimulus intensities either 2 or 4 ms ISIs are effective, due to the faster recovery of the D wave amplitude. Taniguchi et al. used a 200 μs pulse width, while Deletis et al. use a 500 μs pulse width which does have some relation to optimal ISI; also there may be a difference in age between the two studies. Yet as Deletis et al. demonstrate, if the ISI is at a harmonic of the regular I wave intervals, it will require less stimuli to be able to generate I waves and in turn a CMAP, even though this may not be easy to determine in the OR other than by trying differing pulse widths if the response is difficult to obtain [17]. Szelenyi et al. found that an ISI of 4 ms always produced MEPs at the lowest stimulation threshold, yet the difference between the different ISIs was not statistically significant [40].

Another technique used to improve the efficacy of the CMAP is to use a conditioning pulse train [41]. The motor response recorded in the operating room is a combination of responses from multiple motor neuron pools. Each pool is directly activated (D wave) by a single corticospinal axon. If all motor neuron pools are activated simultaneously, it would be easy to just modify the number of pulses in a train in order to elicit the maximum MEP amplitude. In most cases the motor neuron pools do not activate simultaneously when either giving a single pulse or single train of pulses due to dispersion (i.e., uneven conduction along the different fibers) between the fibers. This dispersion has the effect of increasing the time difference between pulses arriving at the motor neuron pool as compared to situations when they were initiated from the cortex. When there is a lesion in the fiber pathway, this dispersion effect increases. Thus, in many cases during surgery, the optimal MEP amplitude is not met due to abnormalities in the spinal cord fibers' conductivity or impaired spinal cord function. The purpose of the conditioning pulse train is to raise the αMN membrane excitability. This prepulse (conditioning pulse) facilitates the generation of the CMAP via the actual test pulse by making it easier for the test pulse to depolarize αMN. This technique works by increasing the membrane excitability (depolarizing the membrane) by both direct activation via the corticospinal tract and also by activating the secondary tracts via interneurons that are not able to be activated by the single train due to anesthesia. In order to optimize the facilitation, the test stimuli need to be applied just when the αMN membrane is maximally depolarized from the conditioning train. Journée et al. developed such a methodology whereby a pretrain is applied prior to the test train to raise the excitability of the αMN [41].

It is known that the motor threshold of a muscle during a voluntary contraction is lower than when that muscle is at rest and that this difference is modulated by both cortical and spinal mechanisms [42]. These voluntary mechanisms used to reduce motor threshold cannot be used when the patient is anesthetized. By using homonymous conditioning (stimulating the same pool at the same site for both the conditioning and test train), there is the potential for a large overlap between the motor pool stimulated with the conditioning pulse and the test pulse. Journée et al. describe two windows for facilitation—(1) with an intertrain interval (ITI) between 10 and 40 ms and (2) with an ITI > 100 ms—and recommend trying the shorter ITI first and then the longer ITI [41].

Transcranial Motor Evoked Potentials

TES and TMS are both used to activate the motor system and elicit MEPs. The two techniques differ in what neural elements are being activated. With electrical stimulation the electrical current flows from the anode to the cathode and the predominant direction of flow is in the radial direction, while for magnetic stimulation the magnetic field passes perpendicular to the plane of the coil which is placed tangential to the scalp (Fig. 7.2). The electric field produced by TMS is perpendicular to the magnetic field and thus tangential to the cortex. Thus for each type of stimulation, the electric field is oriented 90° from each other. For electric field parallel to the neural element, activation is a function of distance and also changes in orientation (i.e., not exactly parallel)

of that element with bends being the most likely sites of activation [43, 44]. The TES response is slightly shorter than the TMS response [45]. The latency difference is a function of the trans-synaptic nature of TMS activation versus the direct activation of CT fibers when TES is utilized. As described above, when TES is applied in the awake animal, there is both a direct response (D wave) from direct activation of the CT axons and also I waves from indirect synaptic activation of the CT axons. Differing orientations of the coil will generate a response at differing latencies with respect to the D wave produced by TES, and even when the coil is in the lateral medial direction and over the central sulcus, a small D wave may be produced [46].

In the 1830s Michael Faraday found that when a pulse of current is passed through a coil of wire, a magnetic field is generated. If a secondary conductor is nearby (within the induced magnetic field), a current is induced in this conductor that is related to the rate of change of the magnetic field [44]. When stimulating the brain using TMS, a coil is placed over the subject's head, and a brief pulse (usually around 100 μs) is passed through that coil generating a magnetic field that is large enough to pass through the subject's skull inducing a current within the brain. It is critical to point out that it is not the magnetic field that is directly stimulating the neural elements, but generating the secondary currents in the neural elements by induction. TMS has been tried during some surgical procedures [47], yet from a practical point of view due to the trans-synaptic nature of CT neuron activation, TMS is not a suitable tool because of the blocking action of anesthetics on synaptic transmission.

Electrical Elicited MEPs

The most common technique to elicit MEPs in the OR is via electrical stimulation applied to the scalp and/or exposed cerebral cortex and then to record the CMAP from the muscles. Using this technique the functional integrity of both the CT and CBT can be continually monitored. The stimulus is applied over the motor cortex and recorded from the end organ (muscle) or directly over the spinal cord. The montage and polarity used to apply the stimulation dictate the focalized nature of the stimulus, the laterality, and the extent of the artifact. For transcranial stimulation the montage can be categorized into bilateral (interhemispheres and midline) or unilateral (intrahemispheric). Using the international 10–20 EEG system, the standard MEP stimulating electrodes are placed over the motor strip and these are approximated with electrodes at positions C_1, C_2, C_3, C_4, and C_z, while for midline stimulation, having the cathode 6 cm anterior to C_z is also one possibility especially when muscle motor twitches disturb surgery. The most common montages are the interhemispheric $C_1/C_2(C_2/C_1)$ and $C_3/C_4(C_4/C_3)$ montages. Making either C_1 or C_3, the anode will preferentially stimulate the CT fibers originating from the left hemisphere, while making either C_2 or C_4, the anode will preferentially stimulate the CT fibers originating from the right hemisphere. The $C_3/C_4(C_4/C_3)$ montage is able to elicit muscle responses in all four limbs but is preferential for monitoring upper limb MEPs, while the $C_1/C_2(C_2/C_1)$ shows a preference for the lower limbs, yet once again is able to elicit responses in all four limbs. The C_3 and C_4 montages have demonstrated the muscle activations with the lowest motor threshold in all four limbs [40] which might make it appear to be the most optimal for most MEP monitoring. An alternative is C_1/C_2 or C_2/C_1. C_3/C_4 and C_4/C_3 montages are known to cause large movement artifact. Instead of a focal stimulation, the stimulus is spread over a much larger area, in turn potentially activating many more fibers. Starting with the $C_3(C_4)/C_4(C_3)$ montage, due to it having the lowest motor threshold is a good solution. Yet, it needs to be kept in mind that this montage has the potential of deeper current penetration, and thus in supratentorial surgeries, such as aneurysm surgery, the stimulation point may be caudal to the site of the surgery and therefore can miss a lesion to the CT. In this case using the $C_1(C_2)/C_2(C_1)$ montage may be more appropriate. Generally in brain surgeries, direct stimulation of the exposed cortex via strip electrode is the method of choice. There are also other more focal

montages such as the unilateral intrahemispheric C_3/C_z and C_4/C_z or the midline C_z/6 cm anterior to C_z. The $C_3(C_4)/C_z$ montage was shown to be appropriate for eliciting upper limb responses, but was very poor in eliciting lower limb muscle responses. The $C_3(C_4)/C_z$ montage is the method of choice when eliciting corticobulbar responses recorded from the vocal muscles[48] or the facial muscles [49]. The focal montage is superior to that of the interhemispheric montages since direct stimulation of the facial nerve itself can occur with the larger spreading montage, without actually stimulating the CBT. This response may also give a false sense of security since the stimulation location may be distal to surgery and thus give false-negative results if the injury occurs proximal to the stimulation point. To exclude the possibility that the current spreads distally and directly activates cranial nerves, and not corticobulbar fibers, the use of single stimulus versus train stimuli is needed [48, 50]. Finally in a rare set of patients, using the midline montage of C_z/+6 cm to C_z may be beneficial for eliciting muscle responses from the lower limbs, yet the stimulus intensity needs to be high.

Stimulation intensity varies along with the MEP technique used. A theoretical calculation by MacDonald et al. showed that using pulse widths between 50 and 800 μs should allow for safe stimulation (below the level of damage to neural tissue) and that using a pulse width of around 200 μs is optimal for energy minimization based on the rheobase and chronaxie of the stimulated neural elements [38]. It should be noted that each patient is somewhat different and patient-specific physiology, disease state, and the patient's own response to anesthetic will affect the optimal stimulus parameters; the above range and values are good starting points. Also, it is important to know the specific legal limitations for your country when applying these tests.

At present there is no generally accepted ISI or train length as a standard for eliciting MEPs. Increasing the overall number of pulses within the train can reduce the stimulation threshold. It is also known that in some patients under light anesthesia, MEPs recorded from the muscles may be elicited by using a single pulse or two pulses, but in general the use of 5 pulses appears to be a good starting point [29]. Yet the use of more pulses (6–8) [51] or less pulses (3–4) [52, 53] is reasonable. Dong et al. [50] reported using 3 pulses when eliciting CBT MEPs. ISI starting points are also variable with the starting point ranging from 1 ms up to 4 ms. Szelényi et al. showed that using an ISI of 4 ms can minimize limb MEP thresholds [40], although using ISIs of 1 and 2 ms has shown to be best for both upper limb and CBT MEPs [38, 50, 54]. It is also worth mentioning that using ISI of 2 ms is recommendable for eliciting CBT MEPs because of their rather short latencies.

In the authors' experience a pulse train of 5 pulses with an ISI of 2 ms and a pulse width of 50 μs is a reasonable starting point for generating limb and CBT MEPs. Yet as discussed by MacDonald et al. [38], individual patient characteristics and anesthetic conditions may require altering of the parameters to get an optimal MEP response.

Direct Cortical Stimulation

In addition to transcranial stimulation for eliciting muscle MEPs, one can also stimulate the brain surface directly. For the purposes of this chapter, we will describe the technique of DCS during aneurysm surgery. Techniques used to map cortex and subcortical brain regions are described elsewhere in this book. For DCS during aneurysm surgery, it is highly recommendable to use a four- to eight-contact strip electrode placed over the specific region of interest—in most cases the precentral gyrus. Thus for MCA aneurysm procedure, the strip would be placed over the lateral motor strip, while for ACA procedures the strip is placed more medially. The cathode is placed at FPz (or as close as possible) with the anode (active, stimulating electrode) being one of the electrodes on the strip. Similar stimulation parameters to TceMEPs are used for DCS stimulation except that stimulation intensity should not exceed 25 mA [55]. In this study published by Szelenyi et al. [55], they were able to record MEPs from DCS in 84 % of cases. Reasons

for not being able to elicit MEPs with this method include seizure, brain swelling, premature aneurysm rupture, subdural scars, and patients with an aneurysm in the posterior circulations (it should be noted that in a small subsection of patients with anterior circulation aneurysms, they did not place electrodes). Dislodgement of the electrode is an issue, yet we have found that once the electrode is in place, and by securing the lead wire with a staple, dislodgement of electrode was not an issue. One of the most frequent problems is the fact that the electrode strip may not be over the motor strip. In some cases the surgeon might try to reposition the electrode, while in other cases this has not occurred and we were not able to elicit MEPs. Szelenyi et al. have recommended that the surgeon use the electrodes on the scalp (the same ones used for TceMEPs) as a guide for placing the strip since this electrode is known to be over the motor strip due to proper scalp measurements at the beginning of the surgery [55].

Once the electrode is placed, we start testing using stimulation intensity of 10 mA and slowly increasing stimulation by 2–5 mA after five trials separated by 0.5–1 s. If no MEP response appears up to 25 mA of stimulation intensity, we switch the stimulating anode to the next electrode. We continue this until all electrodes are tested. The surgeon can continue their surgical exposure while we are doing this. If no response is noted, we let the surgeon know this. The surgeon will then either reposition the electrode strip or continue without DCS MEPs.

MEPs Recorded from the Muscles

Standard MEP monitoring uses the application of a stimulus at the head and the recording of MEPs either from the spinal cord or muscle(s). The stimulus is applied via electrodes placed on the scalp for transcranial stimulation, overlying the dura, or directly on the surface of the brain. For transcranial stimulation, the subject matter of this chapter, gold cup electrodes, needle electrodes, or "corkscrew"-shaped electrodes could be used. Corkscrew electrodes are most often used since they secure to the head by screwing them into the scalp and thus are very stable throughout the procedure and resist falling out. They are also of low impedance (around 400 Ω) which Journée et al. demonstrated. MEP threshold is linearly related to impedance above 460 Ω, while below that MEP thresholds are constant [56]. Both the standard gold disk and the standard needle electrode impedances are 800 and 1,200 Ω, respectively. These electrodes are applied using the standard international 10–20 EEG system.[2] MacDonald et al. recommended placing the central stimulating electrode 1 cm in front of the standard 10–20 system placement of C_1, C_2, C_3, and C_4. This location better corresponds to the motor strip. The FPz electrode is at the standard 10–20 system location [54].

αMN innervated distal muscles receive the highest number of the large CT fibers and should be the matter of choice for recording limb MEPs. The most common muscles monitored are the abductor pollicis brevis, abductor hallucis, anterior tibialis, and biceps brachii. There are some situations where recording MEP responses from segmental muscle may be warranted. Such situations may include far lateral decompressions and foraminotomies. In those cases the surgeon should be informed that MEPs may be less reliable due to the smaller numbers of large CT fibers innervating those muscles and also due to the potential overlapping between spinal roots [57]. Either surface or subdermal needles may be used to record muscle MEP. The authors have found needles to be more stable and secure during long cases, yet care still needs to be taken due to the sharp nature of the needles and the fact they are not always visible to the surgical team. When using needles they should be placed in the muscle bellies about 2–3 cm apart. Table 7.1 lists a set of recommended muscles for MEP monitoring with the most likely innervation from the

[2] Stimulation directly on the brain surface or dura uses other specially designed or modified electrodes and significantly lowers stimulus levels; otherwise the parameters and montage for stimulation are very similar. The technique of direct subcortical white matter stimulation is somewhat different in that the cathode is the stimulating (active) electrode which is different than for eliciting MEPs from the cerebral cortex.

Table 7.1 Common muscle-nerve root mappings

	Muscle	Cranial nerve or root
Corticobulbar	Orbicularis oculi	VII
	Orbicularis oris	VII
	Mentalis	VII
	Cricothyroid	X
	Vocalis	X
	Stylopharyngeus	IX
	Tongue	XII
Upper extremity	Trapezius	C4
	Deltoid	C5, C6
	Biceps brachii	C5, C6
	Triceps brachii	C6, C7
	Flexor carpi radialis	C6, C7
	Flexor carpi ulnaris	C8, T1
	Extensor digitorum communis	C7, C8
	Extensor carpi ulnaris	C7, C8
	Abductor pollicis brevis	C8, T1
	Abductor digiti minimi	C8, T1
Lower extremity	Iliopsoas	L1, L2
	Adductor longus	L2, L3, L4
	Vastus medialis	L2, L3, L4
	Biceps femoris	L5, S1
	Tibialis anterior	L4, L5
	Gastrocnemius	S1, S2
	Abductor hallucis	S1, S2
	Sphincter ani	S2, S3, S4

spinal root (the highlighted muscles are the best for monitoring general CT continuity).

When monitoring muscles innervated by the CBT, the electrode placement varies according to the muscle monitored. For orbicularis oris, orbicularis oculi, or nasalis, it is preferable to use hook wire electrodes. Small needle electrodes placed in the skin parallel to each muscle are also an option, yet the selectivity and recorded EMG response are not optimal. The needles are placed in the muscle at about a 30° angle to the skin. The length of the needle should be around 1 cm. For cricothyroid (CRT) muscle recordings either short needle electrodes or hook wire electrodes can be used. Hook wires are the recommended recording electrode since large surface area electrodes of needles can give false-positive or false-negative results due to the large surface area of the electrodes recording far-field potentials from the neck muscles [48]. This *false data* may indicate that everything is okay with the functional integrity of the nuclei or CBT when it really is not the case. Thus we recommend using the hook wire electrode for recording. Hook wire electrodes placed in the vocal muscle require expertise of either an ENT specialist or anesthesiologists who is trained in this technique. For cranial nerve XII we also recommend using hook wires in the tongue to minimize any damage from the needle due to movement which may lacerate the tongue. For cranial nerve IX we have used both needles and hook wire electrodes in the soft pallet with equally good results.

Stimulation intensity and montage depend on where the stimulation is being applied. The actual stimulation current activating the neuron is the same no matter what montages we used; it is the intervening tissue that determines that actual stimulation current reaching neurons. When the stimulation has to penetrate the scalp and the skull, one needs a much higher stimulation intensity. About 80 % of the stimulation energy is lost in TES. On the other hand, stimulation at the surface of the brain or at the white matter will require much lower stimulation intensities due to no high impedances for passing current. Continuous MEPs elicited from the cortex involve the placement of a strip electrode over the motor area with one of the contacts of stimulating strip as an anode and a contact at FPz as the cathode.[3] For subcortical MEP mapping the active electrode is the cathode just the opposite for eliciting TceMEPs where the active electrode is the anode.

Recording of MEPs is done with a filter setting of 100–3,000 Hz. We choose the 100 Hz high-pass filter to reduce the low-frequency artifact from the stimulator and flatten the response curve on the display. The low-pass filter can range from 750 to 3,000 Hz depending upon the noise, yet as the filter is lowered, the high-frequency components can be lost. It is recommended not to change the filter settings during the case so the shape and amplitude of the waves

[3] One may also use stimulation to map the cortex. This is not the subject matter for this chapter, although the techniques are similar.

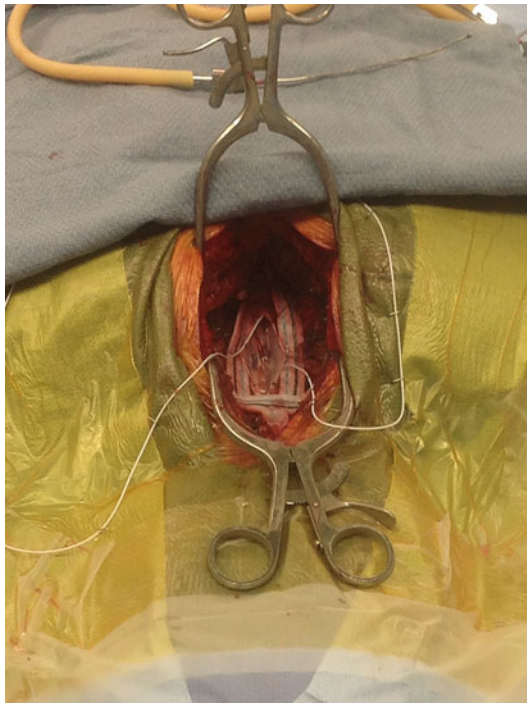

Fig. 7.5 Placement of both cranial and caudal D wave electrodes during an intramedullary spinal cord tumor

are not modified by the filter. In some cases it will be necessary to adjust filter settings if new artifact is introduced during the procedure.

MEP Monitoring Using D Wave

It is possible to record the traveling volley along the CT in the spinal cord during surgical procedures. This is performed by placing a disposable catheter recording electrode either sub- or epidurally and both cranially and caudally to the site of the surgical intervention (Fig. 7.5). A commonly used electrode is the model CEDL-2PDINX-100 (Ad-Tech, Racine, WI) which has three 15 mm spaced electrodes. If it is physically possible, it is better to use for recording contacts 1 versus 3, but in some cases it may not be possible to get all three electrodes to sit on the dura or the spinal cord, or in some cases one of the contacts may fail and then another contact has to be used. D waves are recorded with a 1–1.5 ms/Div time base, a high pass of 50–100 Hz, and a low pass of 1,000–3,000 Hz. Minimizing stimulation artifacts can be achieved by performing ten averages while switching the polarity during each average. The amplitude and latency of the D wave vary depending upon the level of the spinal cord being recorded. In the cervical region the amplitude is greatest with the shortest latency. As the electrode moves caudally down the cord, the amplitude reduces and the latency increases. The reduction of amplitude is due to the reduction of the number of large CT fibers contributing to the D wave amplitude. The latency increase is related to the conduction speed in the spinal cord and the distance from the stimulating to the recording electrodes. Other factors affecting the D wave amplitude are related to the distance of the electrode from the spinal cord, the amount of damage to the CT, and the absolute level of the spinal cord where recording is done. Ulkatan et al. demonstrated that spinal cord anatomic position changes after correction of scoliosis can generate a false-negative D wave amplitude due to changes in the relative position of the epidural electrode to the CT. They also showed that no changes in the muscle MEPs occurred during epidural recorded changes indicating no injury to the spinal cord [58].

Neurogenic Response (Stimulation of the Spinal Cord with Recording from Peripheral Nerve)

Neurogenic MEPs were widely used in the 1990s but have since fallen out of favor due to the fact that there is no evidence that elicited recorded responses are generated by stimulation CT within the spinal cord [2, 59]. This technique requires the placement of stimulating needle electrodes between the spinous processes above the level of surgery (or in cases where the spinal cord or spine is exposed, one can use electrodes placed within the ligamenta flava or directly on the cord itself). For stimulation the cathode is placed caudal to the anode. Recording electrodes are applied over the sciatic nerve (or tibial nerve) in the popliteal fossa. Compound nerve action potentials

(CNAPs) are then recorded. This method is based on hypothesis that CT fibers ending at αMN will be activated via the stimulation; therefore CNAPs represent activity from motor tracts [60]. It is known that antidromic stimulation of the dorsal columns [61] also activates the αMN, via branches of sensory rootlets ending up at the αMN using similar anatomic pathways that convey the H-reflex. Furthermore, other motor tracts beside the CT (e.g., the rubrospinal or vestibulospinal tracts) could activate the αMN. In fact the literature describes patients waking up with pure motor paraplegia who were monitored with neurogenic MEPs with no change in the neurogenic MEP during the procedure [2].

Indications and Contraindications for MEP Monitoring

Any surgery where there is risk of damage to the motor tracts or primary motor cortex should consider utilizing MEP monitoring. These surgeries include neurosurgical procedures in or near the motor cortex or CT in the brain or brainstem, aneurysm clipping, or other vascular procedures that may affect the flow of blood to the motor system, also neurosurgical procedures of the spine, spinal cord, and cauda equina region. Orthopedic surgical procedures including spinal instrumentation for correction of spinal deformities, bony tumors, spinal cord decompression, and trauma and peripheral nerve entrapment correction procedures are possible procedures where MEPs are required. Vascular procedures such as carotid endarterectomy, aortic stenting, aneurysm repair, or spinal AVMs may require MEP monitoring as well. It is important to note that even with the general list mentioned above, there may be other procedures where potential damage to the motor system may warrant MEP monitoring, yet it is critical to note that given the pathology of the patient, the disease, and the goals of surgery, MEP monitoring may not be warranted, and thus every patient should be evaluated prior to surgery to determine if MEP monitoring is warranted.

Even though there is a large group of procedures where MEP monitoring may be warranted, MEP monitoring is not without its complications. Seizures are considered the second highest complication from MEP monitoring. In 2002 MacDonald reviewed the literature and found the seizure rate for TceMEPs to be 0.03 % [62]. When performing direct cortical MEP monitoring during aneurysm surgery, Szelényi et al. found a 1 % seizure rate [50]. The risk for MEP-induced seizures in patients with symptomatic epilepsy was 1.5 % using the high-frequency short-train mapping technique compared to the low-frequency long-train mapping technique which was 9.5 % [63]. Thus, in general, the rate of seizures is rather small, yet in those patients with a history of seizures, or pathology that may enhance its generation, immediate cessation of seizure could be achieved with irrigation of the cerebral cortex with ice-cold saline where application over the cortical surface can halt the seizure within 5–10 s [64]. In addition antiseizure medication can be given. Also, a detailed discussion should be had with the surgeon so they can understand possible risks of monitoring MEPs as well as the risks of iatrogenic injury if MEPs are not used.

For both open cranial and spinal procedures (where direct access to the brain is not possible), Ativan (lorazepam), diazepam, midazolam, all benzodiazepines (barbiturates), or bolus of propofol [65] can help in halting the seizure. Yet, once given a medication it becomes rather difficult to record MEPs due to the cortical inhibition caused by the drug.

Lip and tongue lacerations are the most common complication of MEP monitoring and have a reported incidence rate of 0.2 % [62]. Their most likely explanation is due to the contraction of the jaw musculature triggered through the motor part of the trigeminal nerve or even the CBT pathways [38]. To minimize this complication, it is highly recommended that dual bite blocks be used and placed in between the upper and lower jaw on both sides of the mouth (Fig. 7.6).

Other complications include burns under the stimulating electrodes, movement-induced injuries, transient cardiac arrhythmias, and potential damage to vascular structures with the use of

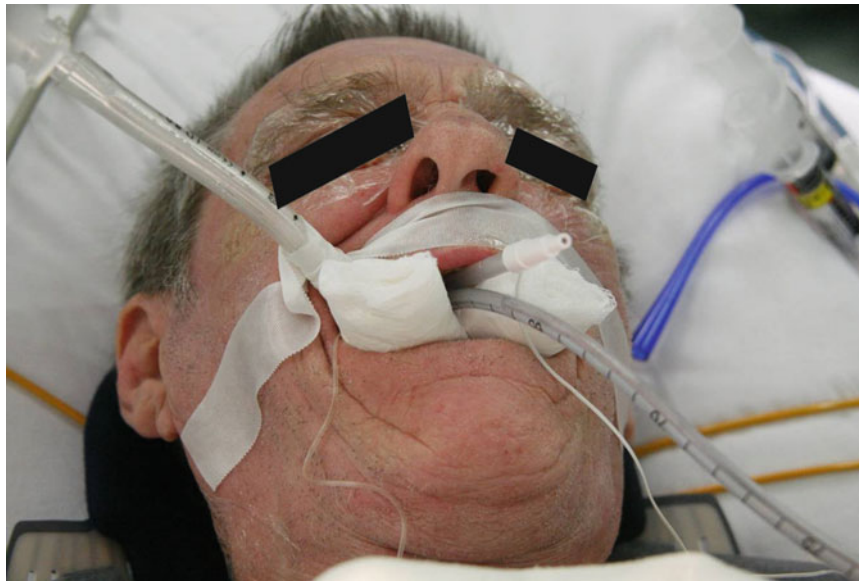

Fig. 7.6 Example of a double bite block to protect against lateral tongue lacerations

electrode placed over the cortex. Burns are due to a buildup of heat between the stimulating electrode or even the recording electrodes and the skin in most cases due to the faulty cautery [62]. In cases where the electrodes are screwed into the scalp too tightly, there may be a cutoff of blood flow and thus no way for heat to be removed causing burns. The more common cause for burns is with equipment failures. If the return current, of the cautery system, or the ground of the IONM system fails, the electrodes, both stimulating and recording, may become those returns causing excessive current to pass through the small stimulating and/or recording electrodes generating burns. Any time a burn is noted during electrode removal, it is recommended that every piece of electrical equipment that comes into contact (either directly or indirectly) with the patient be checked by the hospital's biomedical engineering department/personnel. Once again this discussion should include the benefits and negatives of MEP monitoring during the procedure. Szelenyi et al. [55] stated that 2 of the 100 patients in whom DCS with strip electrodes was used had bleeding from bridging veins damaged during electrode placement. This bleeding caused no neurologic sequel in either patient.

Interpretation and Alarm Criteria

Interpretation of MEP data is dependent on the location of surgery and type of surgery being monitored. What this means is that interpreting changes in MEPs during the monitoring of surgery for cerebral aneurysm appears to be different than monitoring during a scoliosis or other spinal procedures. Yet, there are some key principles when interpreting MEP changes and deciding whether criteria for an alarm have been reached. The primary alarm marker for MEPs is a change in its amplitude. One of the first questions to answer is the time course of the change. Was the change gradual or was it over a very short period of time? Gradual changes tend to indicate something systemic is going on, i.e., changes in the depth of anesthesia or blood pressure. Yet, fast changes may also be related to anesthetic effects, i.e., bolus applications of anesthetics. Thus anesthetic and technical issues need to be evaluated very quickly during the troubleshooting. This is why it is highly recommended to continually review anesthetic concentrations and work closely with the anesthetic team to assure that any application of anesthetic is passed to the IOM team.

In addition to the time course of the change, the focality of the change is also important. In general focal changes are likely due to iatrogenic injury if all other technical factors can be ruled out.

Effects of anesthesia on the MEP have been described earlier in this chapter. Yet, muscle relaxant has a significant effect on the MEP response. It is important to perform a train-of-four (TOF) test when using muscle MEPs in order to assure no muscle relaxant is in the patient's system. Some authors have described acceptable muscle MEPs when using a 2/4 TOF response. The authors find this to be an unacceptable state to monitor MEPs in. Obviously, if there is no response in any of the four twitches, then there will be no muscle MEP; the literature describes muscle MEP responses with at least two out four twitches (see Sloan and Jantti [66]), yet given the variable nature of MEP amplitudes when not stimulating supermaximally when no muscle relaxant is on board, the authors recommend that no muscle relaxant be administered after the initial relaxant used for intubation. It is also important to note the expected length of the procedure since some relaxants have longer half-lives than others and thus will obscure the MEP for longer periods of time. In some instances the surgeons may want to have the muscles relaxed during back exposure or no movements during other exposures. Succinylcholine (SCh) is a common example of a short-acting depolarizing neuromuscular blocking agent that allows for quick recovery and monitoring of muscle MEPs. Yet, it is important to note that in cases of trauma, potassium abnormalities, or other skeletal muscle issues, SCh should not be used [67], as well as other issues where a preoperative discussion with the anesthesiology team can be beneficial. As the muscle relaxant is wearing off, MEPs from the upper limbs will tend to return to full TOF 4/4 sooner than the lower limbs. In addition atrophied muscle or muscles innervated from damaged nerve roots may return at a slower rate than the "normal" tissue.

Basic alarm criteria for MEPs are mostly concerned with amplitude reductions. Criteria range from 100 % loss to a 50 % loss for spinal procedures [4, 5, 37, 67–70] and 50 % loss for cranial procedures [55, 71] for muscle MEPs. For cranial procedures the alarm criteria of 50 % reduction appear consistent and appropriate, yet for spinal procedures the alarm criteria are less concrete. Anesthesia primarily affects the synaptic transmission at the αMN. In addition each TceMEPs trial does not activate the complete pool of αMNs; thus for each trial, the number of excited αMNs is different which is another reason for the variable amplitude. For long cases there is a phenomenon known as potential fade where the MEP amplitudes decrease over time with the stimulus level. This phenomenon is exacerbated by myelopathies. It is important to realize that this is a very slow change and not abrupt.

For epidural recordings (D wave), the alarm criteria are more reliable. The D wave is a function of stimulation at one point on the CT and recording at another point. The D wave is less susceptible to anesthetic effects, and its amplitude is directly related to the stimulus amplitude (for the most part). The D wave amplitude is proportional to the number of fast-conducting corticospinal fibers. In addition it has been shown to be very stable over time [11]. With this in mind, it appears that a 50 % reduction in D wave amplitude is indicative of cord injury and an alarm should be given to the surgical team [29, 37, 38, 72]. Yet as described by Yamamoto et al., during brain tumor surgery a decrement of <30 % is correlated with recovery, while there was a persistent motor deficit when greater than 30 % [73]. This is in concordance with the 50 % alarm criteria used in spinal surgery, given that in cranial surgery only one hemisphere is being affected, and thus one CT is being manipulated. Thus, the surgical region location is important in choosing the appropriate MEP alarm criteria.

In addition to amplitude reduction criteria, there are also stimulation threshold elevation changes and morphology changes. Calancie et al. describe a technique that uses stimulation threshold changes to make predictions and generate alarms intraoperatively [52, 53]. Using this technique the MEP stimulation threshold is determined at the beginning of the case. With this technique, a >100 μV increase in stimulation threshold for greater than 1 h is predictive of a

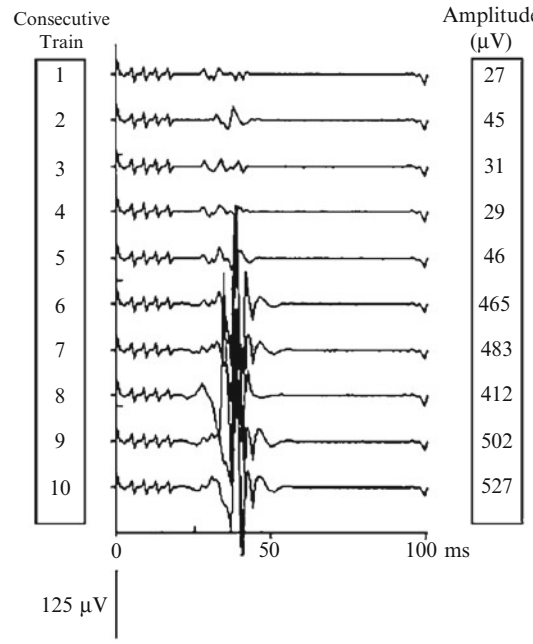

Fig. 7.7 Multi-MEP trials demonstrating the buildup effect. Note by the 6th trial the amplitude of the MEP has increased tenfold. Reprinted from [29]

poor motor outcome. Quiñones-Hinojosa et al. looked at morphology changes in the muscle MEP as an indicator or damage to the spinal cord [71]. Using this method the authors look at the complexity (the number of peaks and troughs in the waveform) as an indicator of outcome. One of the most reliable alarm measures uses the combination of the D wave with muscle MEPs to predict outcome while in addition offering a very stringent alarm criteria [37]. Using this technique a complete loss of the MEP and a >50 % decrement in the D wave result in a complete paraplegia, while a loss of the muscle MEP with no change in the MEP or a less than 50 % decrement will result in a temporary motor deficit [29, 37]. The shortcoming of this technique is that it requires the invasive placement of an epidural electrode which the above two techniques do not. When looking at all of the factors that can affect interpretation of the MEP, it is important to note that each technique is not truly independent. Amplitude and morphology tend to be related. Thus, when the morphology changes, i.e., going from a complex polyphasic wave to a biphasic or monophasic wave, the amplitude of the peak tends to reduce as does the total energy in the wave. Another factor that was mentioned above is the highly likely possibility of incomplete motor pool activation. Repetitive trials can help overcome this incomplete activation (Fig. 7.7). Using the paired-pulse technique of Journée et al. can help to minimize the false-negative rate experienced in the OR [41].

Conclusion

Monitoring of the motor system, as in all IOM, is not simply looking at waveforms. Each modality, including MEP, has special conditions that can confound the interpretation. The physiology of the motor system adds a complexity to MEP monitoring by adding variability to each trial. Understanding this physiology is critical to properly performing and interpreting the MEP intraoperatively.

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Electromyography (EMG)

8

Kenneth Mancuso, Amit Prabhakar, Jonathan Lissauer, Alan David Kaye, and Scott Francis Davis

Introduction

The recording of compound muscle action potentials (CMAPs) in response to spontaneous or electrically stimulated cranial nerve, spinal nerve, or ventral root activation is known as intraoperative electromyography (EMG) [1]. EMG is one of the most useful modalities for intraoperative monitoring (IOM). It is one of several methods of monitoring neurologic function, including the electroencephalogram, sensory evoked potentials, motor evoked potentials, transcranial Doppler ultrasound, cerebral oximetry, and jugular oxygen saturation [2].

Electromyographic monitoring of motor nerves during surgery allows early detection of surgically induced nerve damage as well as confirmation of the functional status of the nerve. EMG was first utilized intraoperatively in the 1960s for the preservation of facial nerve function especially during procedures involving vestibular neuromas [3, 4]. As surgical techniques improved, EMG monitoring soon became used for assessing and preserving the function of other cranial nerves [5]. In addition to its use in patients undergoing surgical procedures that place the cranial nerves at risk, it has become widely used for the IOM of spinal nerve roots during surgeries to correct various spinal deformities by providing a method of detecting changes in neural function intraoperatively [6]. One of the most popular uses of EMG in the operating room is to test the placement of pedicle screws [7, 8].

Anatomical and Physiological Basis of the EMG

A myotome is the muscle or muscle group innervated by a single nerve root. Myotomes are the motor complement to dermatomes, and myotome

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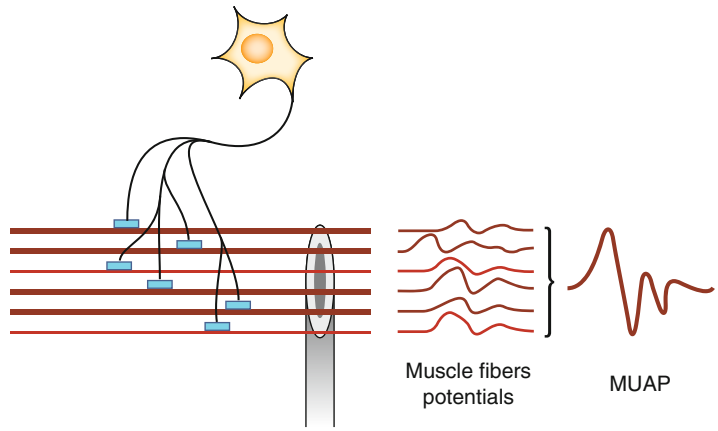

Fig. 8.1 A motor unit is shown with a recording electrode in proximity. Individual muscle fiber potentials are recorded in sum as the motor unit action potential (MUAP)

distributions are also quite variable between individuals. An individual muscle may be part of more than one myotome, meaning that more than one nerve root may contribute to its innervation [1]. A single axon may innervate few or many individual muscle fibers. The axon and all of the muscle fibers it innervates are known as a motor unit. Stimulation of an individual axon sufficient to reach the threshold for action potential firing will activate a motor unit. The individual muscle fiber action potentials can be recorded in sum and this waveform is the motor unit action potential (MUAP) [9]. The MUAP is the basis of the EMG recording (Fig. 8.1).

EMG recordings are made from either surface electrodes or needles placed directly into the muscle(s) of interest [9]. Intraoperative EMG testing can involve passive muscle recordings for the purposes of detecting cranial nerve or nerve root irritation (known as spontaneous EMG or S-EMG) or may involve electrical stimulation of neural elements or hardware for the purposes of assessing function (known as triggered EMG or T-EMG).

Spontaneous EMG

Spontaneous EMG is used as a means of monitoring cranial and spinal nerves during surgery. The premise is that impending injury to these structures by stretch, compression, or other forms of mechanical irritation will cause them to increase firing which is detectable as CMAPs in the monitored muscle groups [10–14]. Ischemia usually does not induce action potential firing and thus is poorly detected by EMG. Proper selection of muscles to monitor is key to the success of S-EMG monitoring.

Many of the cranial nerves that are routinely monitored with EMG have sensory or autonomic components in addition to the monitorable motor component. In these cases, EMG is used as a sentinel for function of the entire nerve, even if the motor component is the smallest functional component of the nerve. If the motor division of the cranial nerve includes branches, it is appropriate to monitor the muscles innervated by each branch whenever possible.

Spinal nerves are mixed (sensory and motor) nerves that may be monitored for irritation with spontaneous EMG [11, 12, 14]. Spontaneous EMG monitoring differs from other intraoperative neuromuscular monitoring modalities in that the expected or normal state is the lack of response due to the absence of any muscle activity [12]. This indicates that a normal healthy nerve has not become activated as a result of surgical stimulation.

Interpretation of intraoperative EMG depends on a familiarity of the various types of firing patterns commonly seen. Various responses may be seen during EMG monitoring. Some patterns of spontaneous activity are suggestive of nerve root irritation or injury. If preexisting

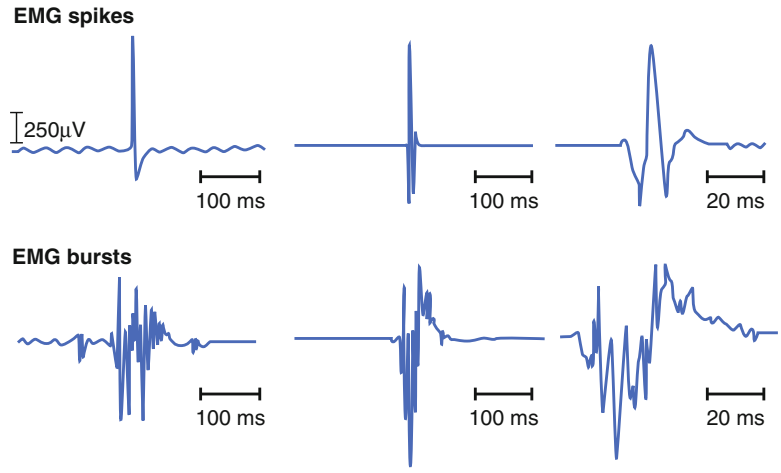

Fig. 8.2 An example of EMG spikes (*upper panels*) and bursts (*lower panels*)

nerve root irritation is present, the baseline EMG recording will often contain low-amplitude periodic firing patterns [1].

The clinical significance of the EMG firing pattern can be generally considered proportional to the frequency, amplitude, and persistence of the firing. Waveforms occurring at high frequency and amplitude indicate multiple motor units involved and a higher likelihood that the firing pattern is a warning of an impending injury. The correlation of EMG activity with a surgical event (such as retractor placement or hardware insertion) suggests a causative event and reversal or cessation of the event should result in a return to the baseline EMG pattern. Persistence of EMG firing beyond cessation of the causative event is worrisome and suggests that injury to the nerve may have already occurred.

Random activation of one or a few motor units during surgery may occur with incidental contact with the neural elements and is not considered clinically significant. These waveforms are termed spikes when the activity of one motor unit is recorded or bursts when the waveform is generated by activation of several motor units (Fig. 8.2). It is important to remind ourselves that the MUAP or spike is actually the recording of a compound action potential consisting of the individual muscle fiber action potentials. As such, its morphology is distinctly different than a single action potential generated by a muscle cell or a neuron. Specifically the duration of the event is longer, often several milliseconds. These waveforms are also polyphasic as opposed to biphasic. Spiking or bursting in the EMG indicates proximity to the neural elements and may be a useful information to the surgeon while navigating the field.

Sustained activation of multiple motor units results in firing patterns with a greater degree of clinical significance. EMG "trains" are repetitive prolonged firing of one or more motor units, lasting from seconds to minutes [9]. The length of time a nerve is activated is dependent on the degree of nerve irritation [15]. Significant nerve irritation or nerve damage can produce neurotonic discharges in which no individual muscle action potentials are distinguishable [13] (Fig. 8.3). These two patterns of activity are ubiquitously recognized as warning criteria for nerve or nerve root injury and should be reported to the surgeon immediately.

The use of audio output of the EMG signal is very useful to the surgeon in providing real-time data for both navigating the surgical field as well as warning of impending injury to the neural elements. The use of real-time audio feedback enables the surgeon to respond with immediate correction or to be more aggressive with his approach based on the data.

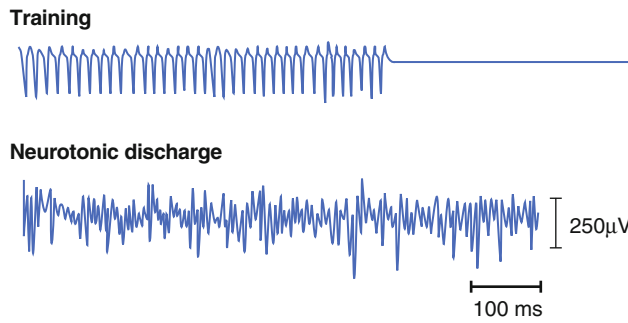

Fig. 8.3 An example of training and neurotonic discharge in an EMG recording

Triggered EMG

Triggered EMG is used for three primary reasons: to identify a nerve or nerve root of interest, to assess the functional integrity of a nerve or nerve root, and to assess the placement of pedicle screws.

Identifying Nerves and Nerve Roots

Direct electrical stimulation of a nerve or nerve root can assist in its identification. Due to redundancies of innervation patterns, accurate identification of a branch of a cranial nerve or the level of a nerve root requires specific monitoring of CMAPs using a bipolar recording montage (see Chap. 4).

Stimulating a nerve or nerve root directly is best accomplished with a handheld bipolar probe. A bipolar probe will reduce the size of the current field and increase the specificity of stimulation. Square wave pulses with a pulse width of 50–100 μs are delivered at a rate of approximately 2 pulses per second.

A healthy neural tissue should stimulate at an intensity of less than 2 mA and produce a recordable CMAP. When setting the display parameters, it is important to keep in mind both the latency and amplitude of the expected response. Most CMAPs can be several millivolts in amplitude. The latency is dependent on the distance between the stimulation and recording site. For most cranial nerve monitoring, the latency will be between 2 and 10 ms. For spinal nerve roots, the latency is longer.

Assessing the Functional Integrity of a Nerve or Nerve Root

Direct electrical stimulation is also used to assess the health and function of a nerve root. Healthy nerves have a stimulation threshold well under 2 mA and often under 1 mA. The use of direct nerve stimulation to provide diagnostic information concerning cranial and spinal nerves is based on the premise that previously injured or chronically compressed nerves have a higher electrical threshold for activation [16]. This concept has been extended in the use of pre- and post-tumor resection thresholds for providing prognostic information about cranial nerve function [17, 18]. There are technical considerations that should be taken into account when stimulating nerves directly in the surgical field that may reduce the sensitivity and specificity of stimulation. As mentioned above, the use of a bipolar stimulating electrode is preferred for the task of direct nerve stimulation. Furthermore, it is imperative that the surgical field is dry to prevent the shunting current away from the intended stimulation target. Current shunting may result in failure to stimulate the structure or create an artificially high stimulation threshold.

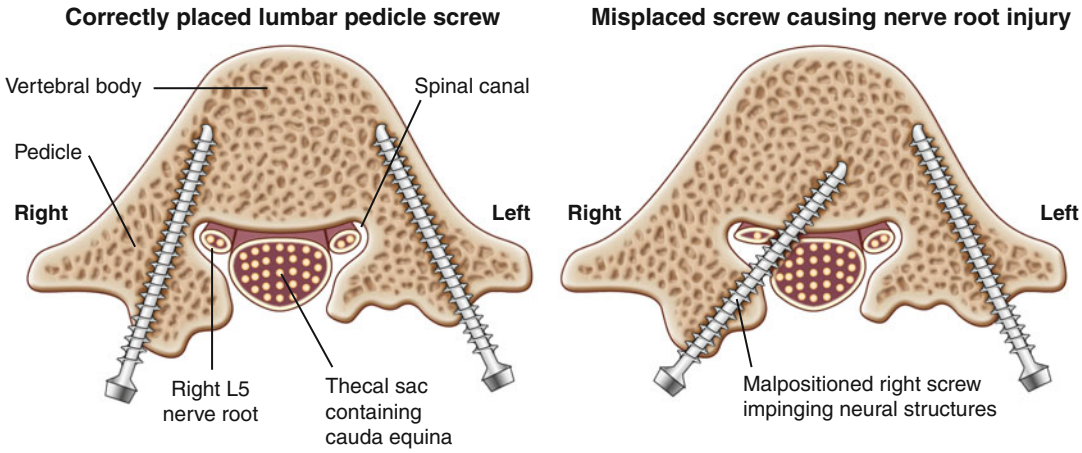

Fig. 8.4 Correctly placed and misplaced lumbar pedicle screws

Stimulating Pedicle Screws

Pedicle screws are used in surgeries for the correction of spinal deformity as well as for procedures to decompress neural elements and reduce pain and neurologic symptoms. The function of pedicle screws is to stabilize vertebral bodies following laminectomy and/or discectomy until bony fusion of the adjacent levels is complete. Pedicle screws are placed through the pedicle and into the cortical bone of the vertebral body with care not to breach the pedicle and enter the vertebral canal causing spinal cord or nerve root injury (Fig. 8.4). Blind placement of pedicle screws without EMG or imaging guidance carries a higher risk of neurologic injury [19, 20]. Neurologic injury resulting from misplaced pedicle screws can be either radiculopathic (involving a nerve root) or myelopathic (damage to the spinal cord).

Accurate placement of pedicle screws is optimized by the use of both intraoperative imaging and electromyographic guidance [7, 10, 14, 21–25]. Imaging techniques have evolved from plain radiographs to fluoroscopic guidance and most currently intraoperative computerized tomography (CT) techniques [26–28]. Stimulation of pedicle screws cannot determine good bone purchase, but instead can indicate the presence of a pedicle wall breach with reasonable sensitivity. This technique is best used together with imaging guidance and visual inspection.

The premise behind the electrical stimulation of pedicle screws to determine malpositioning relies on the fact that bone is an electrical insulator and will limit the amount of current transfer between the stimulated screw and the neural elements. A breach in the pedicle wall provides a low resistance conduit of electricity from the electrified screw to the nerve root, which is recordable as a CMAP in the myotome of that nerve root (Fig. 8.5). If a large amount of current is required for activation of the nerve roots, it is a reasonable assumption that the bone is intact. Lower stimulation thresholds indicate a potential breach.

The stimulation of pedicle screws is commonly performed with a monopolar handheld stimulator with a ball tip. The ball tip is designed to make good contact with the head of the screw. A subdermal needle electrode is used as an anode and placed at a distant site such as over a bony prominence or in the abdomen. Square wave pulses of constant current are used having durations of 100–300 μs delivered at a frequency at approximately 2 pulses per second (avoiding factors of the line frequency). Since determination of the stimulation threshold is the aim of pedicle screw testing, it is imperative that stimulation

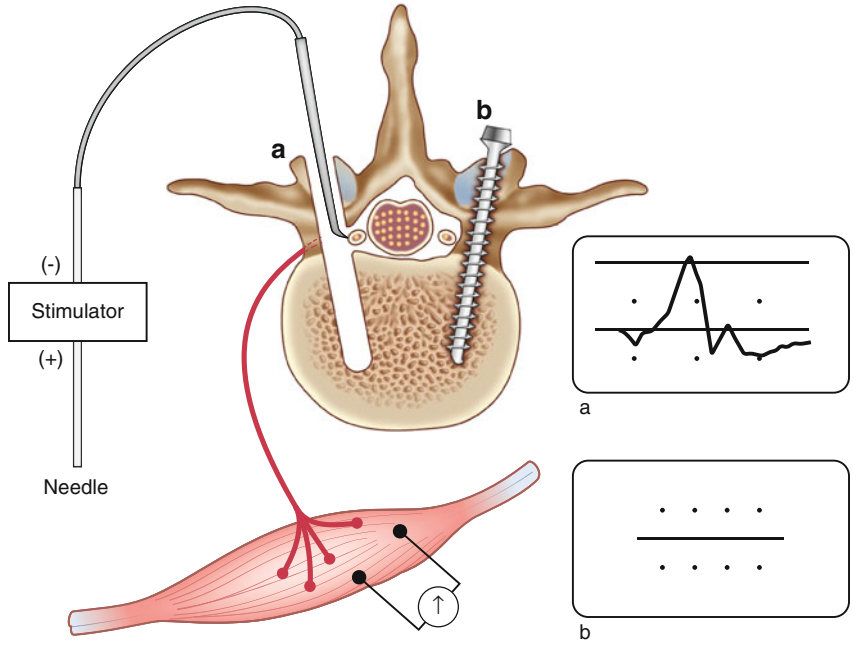

Fig. 8.5 (**a**) The stimulation of a screw or hole that is malpositioned resulting in a pedicle wall breach will provide a conduit for nerve root activation and a recordable CMAP. (**b**) A pedicle screw or hole that is placed correctly without a breach will not result in a recordable CMAP at low stimulation intensities

starts at 0 mA and is advanced in increments of 0.5–1 mA until a response is seen. A record of the response is made (screen capture or save function) along with the stimulus threshold, and this is communicated with the surgeon.

Stimulation of the pedicle screw provides post hoc evaluation of pedicle screw placement. Another commonly used technique is the stimulation of the pilot hole prior to screw placement. Proper stimulation of the hole requires good technique in order to provide an accurate indicator of a pedicle wall breach. Proper technique involves turning the stimulator on and setting the intensity to 8 mA while moving the probe slowly up and down along the pedicular hole. If a CMAP is recorded during stimulation at 8 mA, the intensity should be reduced and the stimulation threshold should be documented. Continuous stimulation during pilot hole formation using either an alligator clip attached to an awl or pedicle access needle (PAC) or a commercially available stimulating PAC is an increasingly popular way to increase the accuracy of screw placement [29].

The interpretation of the pedicle screw testing data is not necessarily well agreed upon with some reports advocating an absolute acceptable threshold of 10 mA and other more recent reports, describing the probability of having a misplaced screw when the threshold is in a particular range [23, 25, 30–32]. The reader is encouraged to explore the primary literature as it relates to this topic. The current trend in thinking is that the probability of detecting a medial wall breach increases with decreasing stimulation thresholds. A CMAP recorded at thresholds under 5 mA are highly specific for a breach (very few false positives) but poorly sensitive (a large number of false negatives) [25, 32]. The sensitivity is higher when CMAPs are recordable at stimulation intensities under 3 mA. The variable sensitivity of pedicle screw stimulation is the reason that it should remain an adjunct to imaging and not solely used to detect a pedicle wall breach.

Other factors to consider when evaluating pedicle screw testing data include consistency of thresholds between sides and vertebral levels as

well as the age and sex of the patient and apparent quality of bone on examination. There is a large incidence of poor bone quality among older patients, especially females. The existence of microfractures in these patients may lower the stimulation threshold to suspect levels but should do so uniformly among sides and levels. When lower stimulation thresholds are seen on all screws, it is reasonable to assume that bone quality is playing a role. With that said, outliers compared with data obtained contralaterally or from adjacent levels should be considered clinically significant.

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Brainstem Auditory Evoked Potentials

9

Jonathan Norton

The auditory brainstem evoked potential (ABEP) is probably the potential with the most names and acronyms in the field. The potential is also commonly known as the auditory brainstem response (ABR), the auditory evoked potential (AEP), the brainstem auditory evoked potential (BAEP), and the short-latency AEP [1]. However, despite its large number of names, it is one of the simpler potentials recorded in the operating room. Auditory stimulation results in a train of evoked potentials that extend for a prolonged period of time (up to 250 ms). However in the operating room, we are predominantly concerned with the short-latency, subcortical responses, often termed the short-latency auditory evoked potentials. Colleagues in audiology use the longer latency potentials in their assessment of hearing [2].

Indications

The BAEP (Brainstem Auditory Evoked Potential) is widely used to monitor the integrity of the auditory nerve, but also often as a marker for brainstem health. Outside the operating room, it has been used to assist decision making concerning brain death although this is certainly not a standard procedure at this time [3]. In order to understand the indications for BAEP monitoring, we must first understand both the anatomy and the physiology of this potential. For the sake of simplicity, we will not discuss the generation of an action potential in the cochlear and auditory nerve; instead the reader is referred to either general physiology texts or to audiology texts such as *Audiology: The Fundamentals* Bess and Humes [2]. Thus far, the nerve has been referred to as the auditory nerve. Formally it is the auditory portion of the 8th cranial nerve (CN VIII) [4]. The other portion of the nerve is the vestibular portion, for which no effective intraoperative monitoring techniques exist. The intracranial portion of the nerve runs in close proximity to CN VII [5]. The auditory pathway consists of the classical lemniscal pathway (considered here) and an extralemniscal pathway (Fig. 9.1). The lemniscal pathway generates the short-latency AEPs through a series of "relay stations." From the auditory nerve, the first synapse of the lemniscal pathway is the cochlear nucleus. It is at this point that a bilateral response is first generated. Fibers exiting the cochlear nucleus either cross the midline and project to the contralateral superior olivary complex (SOC) or remain uncrossed and project to the ipsilateral SOC. The SOC then gives off projections that travel to the inferior colliculus in a fiber tract known as the lateral lemniscus. It should be noted that there is a second bilateral projection from the inferior colliculus to the corresponding inferior colliculus on the contralateral side. The inferior colliculus sends projections to the ipsilateral medial geniculate nucleus of the thalamus. From the thalamus, fibers

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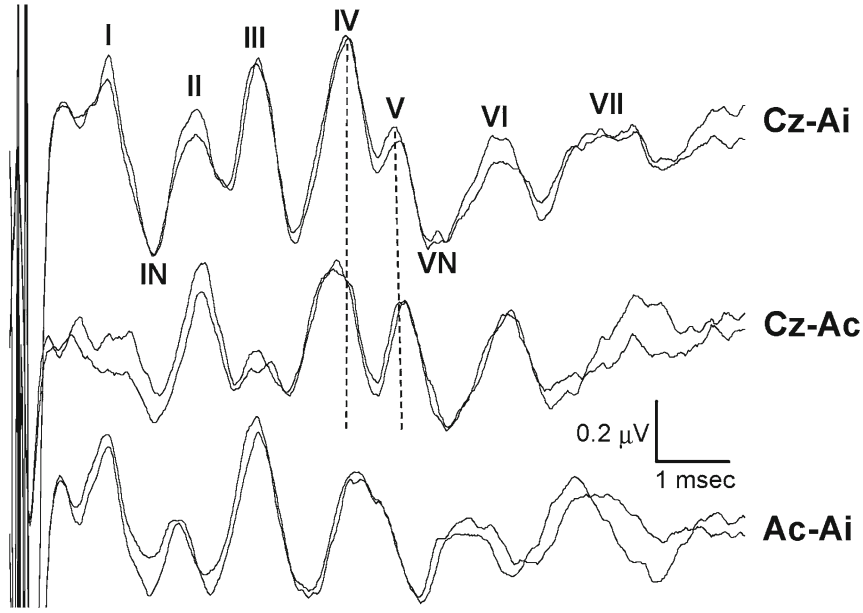

Fig. 9.1 The waveform of the BAEP can be recorded in three different montages, through the use of just three electrodes. Peaks I through to V are visible on the ipsilateral recording and II–V on the contralateral recording. Recordings from the two earlobes also allow all five peaks to be seen. The figure usefully illustrates the comparative ease of distinguishing different peaks depending on the montage selected. In practice, all of these can be easily run at the same time (from the 5th edition of Aminoff. Figure 23.6)

travel as the auditory radiations to the auditory cortex in the temporal lobe [4, 6]. This very brief review of the anatomical path of the BAEP allows us to understand some of the indications for the intraoperative monitoring of the potential.

Tumors of CN VIII are known by a number of names, acoustic neuroma, vestibular schwannoma, and vestibular neuroma. For the most part, these tumors are derived from Schwann cells on the vestibular branch of CN VIII, so a vestibular schwannoma is possibly the best description [7]. Rarely the same tumor type can occur on the auditory portion of the nerve. These tumors are generally benign and slow growing. Many cases are treated with gamma knife technology as an alternative to surgery. Because both the vestibular portion and the auditory portion of CN VIII run so closely together for most of their length, monitoring of the BAEP is indicated in any tumor resection of CN VIII if the intent is to preserve hearing. Since posterior fossa craniotomy also places the brainstem at risk, the BAEP is also monitored as a way to detect brainstem ischemia. Bilateral BAEPs should always be recorded when possible. Although it is ideal for the IOM clinician to be able to participate in preoperative planning of these surgeries, in some instances this is not possible. If you are able to be part of the team preoperatively, it is helpful to know if there is any serviceable hearing left and to what degree. The patient's facial nerve function can also be documented at this time since facial nerve monitoring will be performed during this type of case as well. In non-hearing preservation surgery, there is of course no need to monitor the BAEP ipsilaterally.

Microvascular decompressions (MVDs) for a number of conditions also can pose a risk to CN VIII, either directly or through ischemic changes. MVD of CN VIII is indicated in cases where the patient suffers from either disabling tinnitus (auditory portion) or positional vertigo (vestibular portion). BAEP monitoring should also be considered for MVD procedures to relieve trigeminal neuralgia (CN V), hemifacial spasm (CN VII), or glossopharyngeal neuralgia (CN IX) [1, 7–9].

Space-occupying lesions of the fourth ventricle can disrupt brainstem function. Because of its many relay stations within the brainstem (it is called the *brainstem* auditory evoked potential after all!), the BAEP is a useful monitor of brainstem health. However, it is important to remember that the brainstem performs a wonderful variety of neural functions and the BAEP only directly assesses a small function of the brainstem [10].

Tumors of the cerebellar pontine angle (CPA tumors) remain the most often indication for BAEP monitoring. Surgery to remove these tumors requires the neuromonitorist to bring their full armamentarium to the case, and that will undoubtedly involve the BAEP as well as EMG monitoring of the lower cranial nerves [11].

Peaks, Generators, and Blood Supply

The BAEP has five peaks or waves that are monitored in the intraoperative setting (Fig. 9.2) [12–14]. The peaks are named peak I through to peak V (wave is often substituted for peak). Peak I is generated in the distal auditory nerve, and there is very little controversy about the origin of peak I. However, for the rest of the peaks, the situation is a little more complicated as each peak has more than one potential generator. We will initially consider the primary generators or at least the generators that are most commonly considered the primary generators. Peak II is generated from the auditory nerve, but in this case the intracranial portion is also called the proximal portion of the auditory nerve. The third peak, peak III, is the first that originates from the secondary neurons, meaning that they are the first peaks for which a synapse is involved. The caudal pontine tegmentum is the principal generator of peak III, as well as the negative peak between peak III and peak IV, sometimes known as IIIa. There is some evidence however that there is a contribution from the cochlear nucleus to peak III as well as a contribution from the ascending activity within the lateral lemniscus. Peak III is usually not altered in individuals with lesions in the upper or middle pons, or even the mesencephalon, which is evidence that the generator lies caudal to this point. The most likely generator for peak IV is the SOC, but there is no conclusive evidence to date for a precise origin to be determined. The lateral lemniscus remains a candidate for the generator of peak IV. Peak V, the last of the BAEP peaks, is generated predominantly by the contralateral mesencephalon, specifically the inferior colliculus. The lesions of the pons and mesencephalon frequently affect peak V first in the time course of the disease, and as such, this peak may be abnormal in patients undergoing surgery even when the tumor is considered to be relatively small [13]. Later peaks are not considered as part of the BAEP for the purposes of IOM at present.

Preoperative Considerations

Preoperatively, the neuromonitorist must determine the baseline hearing of the patient. Often audiologists assess this formally before the surgical procedure is planned. An appropriate stimulation level for intraoperative BAEPs can then be determined. Preoperative BAEPs may be helpful if there is time to obtain one. This is one of the easier evoked potentials to perform on an awake patient. Very few people find the process uncomfortable [3, 15]. Gathering these data before the surgery may give insight into any apparent abnormalities in the operative baseline and help distinguish between preexisting pathology and a technical issue.

The size of the ear canal and whether it is occluded with earwax should also be determined prior to surgery. The presence of wax in the ear canal results in a conductive hearing deficit and will impact the monitoring data. If determined during the preoperative visit, the patient can be asked to clean their ears prior to surgery. If not discovered until the patient is seen in holding, then an ENT consult should be considered for wax removal prior to surgery.

The anesthetic regiment has little to no effect on the potential, and so any concerns or discussions with the anesthesia members of the team are more likely to focus on modalities other than the BAEP [8].

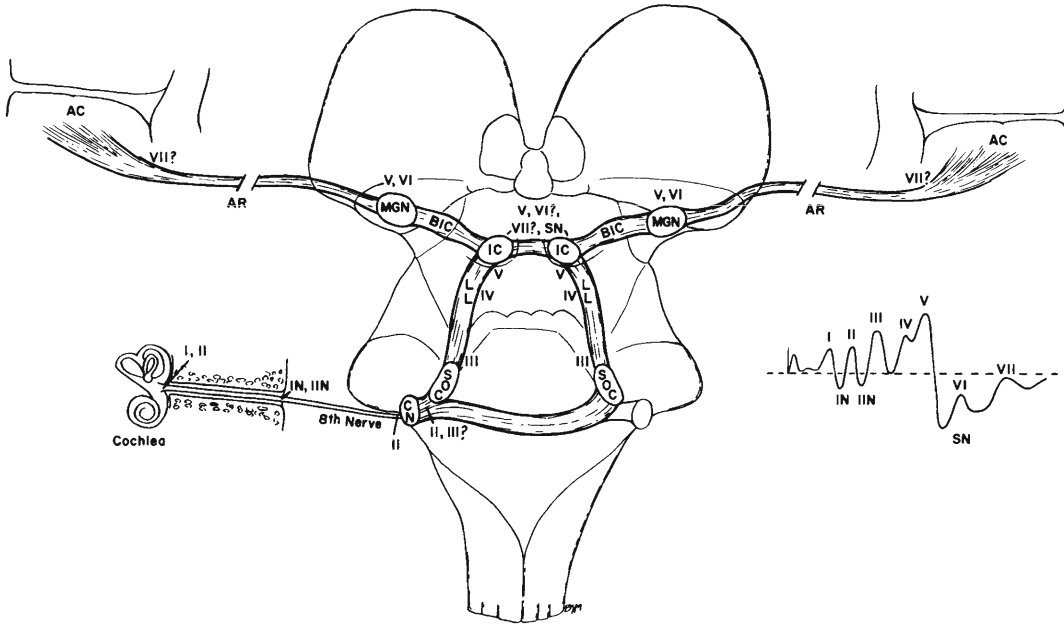

Fig. 9.2 The likely generators within the brainstem of auditory evoked potentials. The roman numerals refer to the individual peaks within the potential. *CN* cochlear nucleus, *SOC* superior olivary complex, *LL* lateral lemniscus, *IC* inferior colliculus, *BIC* brachium of the inferior colliculus, *MGN* medial geniculate nucleus, *AR* auditory radiations leading to AC, auditory cortex (from the 5th edition of Aminoff. Figure 23.16)

In the operating room, stimulation is usually provided through ear inserts, placed into the ear canal and connected to the electromechanical stimulator through relatively rigid tubing of a known length. The neuromonitorist in the operating room must therefore determine an acceptable location to place the stimulators that will allow them to move with the patient but out of the way of the surgeons. In practice I find affixing them to the Mayfield clamp the most reliable way of performing this important step of setup. Replacing the ear inserts if they fall out during a case can be difficult and is not going to win you much appreciation from the rest of the team.

Stimulation

Clicks

Like any evoked potential, the BAEP is a time-locked (and averaged) response to a given stimulus. In this case, the stimulus is a broadband click, generated by an electromechanical transducer. In the outpatient setting, the stimuli are pure tones of known frequency and are usually generated in the ear pieces of headphones. The objective of the clinical BAEP is to diagnose specific hearing deficits, while in the OR, the objective is to preserve gross hearing. This is the reason broadband clicks are used over pure tones in the OR. Since the large headphones are impractical in the operating room, they are replaced with small transducers and the click is delivered to foam ear inserts through stiff rubber tubing. The length of the tubing is known and therefore imparts a fixed and known delay between the electrical pulse that generates the click, which triggers the recording system, and the delivery of the click to the ear [15]. In most cases, this is a 1 ms delay. The tubing is stiff to allow for reliable delivery of the stimulus to the ear. Care must be taken that the tubing is not pierced which will reduce the amplitude of the delivered click or clamped or kinked which may prevent delivery of the click altogether [16]. It is always worth checking this tubing after positioning of the patient but before the drapes are placed. Once the inserts are placed,

sealing the ear canal with bone wax and placing Tegaderm over the ear will prevent fluid from entering.

Each click is generated by the movement of a membrane in the transducer either towards or away from the ear drum. The direction of movement is controlled by simply changing the electrical current driving the transducer. Since the space between the membrane and the eardrum is enclosed and air cannot readily escape, movement of the membrane towards the ear drum condenses the air in that space. This type of click is therefore known as a condensation click. Similarly movement of the membrane away from the eardrum will reduce the air pressure (making it more rarefied) and so is known as a rarefaction click.

In practice, both types of click sound the same on a behavioral level. Some individuals show a better response to one form of the click or another, and in those instances the optimal form should of course be used. However for many people, there is no difference in their response (at least meaning that good, monitorable signals can be obtained from either polarity), and so the choice is left to the person running the case. It has been noted that condensation clicks can enhance peak V while rarefaction clicks may enhance peak I.

There is one further option available on most modern IOM and EP machines, and that is to alternate the clicks. Alternating clicks can sometimes improve the amplitude and discrimination of the peaks (see below) and it also removes or reduces the artifact substantially. The removal (or reduction) of the artifact has its supporters as well as its detractors. As ever, the artifact serves to confirm that a stimulus pulse has been applied, although in the BAEP it is possible to get an artifact with the ear tubes out of the ear. However in general, the amplitude of the artifact will be an indicator of the amplitude of the stimulation (at least the electrical trigger to the electromechanical transducer).

Parameters

There are, with all evoked potentials, a number of parameters that can be varied for the BAEP. For the BAEP, these parameters are stimulation rate, stimulation amplitude, and the polarity of the clicks as discussed above.

The stimulation amplitude, measured in decibels (dB), determines the size of the evoked potential recorded. This is not a linear response, however, as stimulation below the hearing threshold will not result in any response. Above that level increases in the amplitude will give an increase in the amplitude of the response. Conductive hearing deficits have a similar effect on the recorded responses as reducing stimulation intensity.

Stimulation rate has a profound effect on the amplitude of the response. As ever with IOM, there is a desire for real-time recording and interpretation, and the BAEP can be recorded adequately with stimulation rates between 5 and 50 pulses per second (pps). So why do many groups tend to work towards the lower end of the spectrum? Especially as each patient is their own control and so there is no need to conform to laboratory standards. There is an optimum frequency that compromises between speed and quality of response. Above 10 pps, the response tends to lose amplitude so most clinicians work around the 10 pps range, avoiding of course exact multiples of the local line frequency.

Recording

The recording settings for the BAEP in the operating room are similar to those in the outpatient clinics. The high-pass filter is typically set at 30 Hz but can be increased to 100 Hz if required to reduce line noise. The low-pass filter is set at 2 kHz or a similar frequency depending on individual machine specifications. The small size of the cortically recorded responses dictates that the larger number of responses needs to be accumulated to typically obtain reliable and repeatable records. It is not uncommon to need 1,000–3,000 averages to obtain a quality signal. However, with some optimization of the stimulus, environment, and recording conditions, it is possible to need less than 200 averages in some cases. There is considerable value in trying to use the fewest averages possible to get good responses [16].

Montages

The generators of the short-latency BAEP (see below) are all deep within the brain, and so in general the recording montage is actually relatively unimportant in IOM. Since the electrodes do not move during a case and the patient serves as their own control, there is some latitude in montage selection for IOM, but not in outpatient clinical practice [15]. Probably the most usual configuration is using three electrodes: the two ear lobes (A1 and A2) and the vertex (Cz). Since the generators of the peaks are all distant to these recording sites, it is obvious that the exact locations are not overly important. If I am only recording the BAEP, I do not measure the vertex, but am happy to locate that electrode by "eyeball" and to move it to accommodate surgical considerations. A common alternative to the ear lobe is to use the mastoid. In these instances, the recording montage is configured A1-Cz and A2-Cz. It is always worth displaying both the ipsilateral and contralateral derivations. Peak I will only be visible from ipsilateral recording (often termed Ai, i for ipsilateral and therefore Ac with the c for contralateral). In contrast, peak V is most clearly visible within the IV/V complex from the contralateral recordings.

Troubleshooting the BAEP

Within the field of IOM, the BAEP is probably the most robust signal that is recorded. Anesthesia has little to no effect on the waveforms, and temperature variations within the normal physiological range have no effect on the latencies, although cold irrigation may increase latencies for a brief period of time. Variations in blood pressure have little effect on the BAEP as well [8].

The aspects of surgery have significant effects on the BAEP though. As with most IOM signals, monopolar cautery prevents the recording of the signal and can in some instances lead to a short-term saturation of the amplifiers. Bipolar cautery can be used during recordings at times but will often lead to interference on the recordings. It is less common that amplifier saturation will occur with bipolar cautery, but it should always be considered a possibility if there is a sudden disappearance of the waveform [17].

With many of the surgical procedures for which the BAEP is warranted, there is a considerable amount of bone drilling to be performed. Interference from the high-speed drill is a result of the vibration of the bones within the skull and less so from any electrical interference if an electrical drill is used. For an accurate BAEP, the drilling must have ceased as the vibration may result in disappearance of all waves of the BAEP. It is important that this information is communicated to the rest of the team before the procedure commences. A further potential issue that occurs during bone drilling is the large amount of irrigation that can be used. This fluid can easily find its way into the ear and even through routes that seem highly unlikely. Fluid in the ear canal will result in an attenuation of the amplitude and increase in latency of peak I. The best solution for this problem is to prevent it from happening by trying to ensure that the ear canals are watertight before draping.

As mentioned previously, care must be taken that the tubing between the ear inserts and transducers is patent and not kinked. The transducers do have some mass and will tend to pull down and so should be fixed to something that should move with the patient. Much brainstem surgery involves patient movement to obtain the best surgical approaches and so the transducers should be fixed to the head holder.

Interpretation and Alarm Criteria

The BAEP within the operating room has a number of measured and useful parameters. Both latency and amplitude are used as alarm criteria, but the alarm criteria will be specific for any given surgery. However some principles can be used as discussed below. The first parameter to be considered is the latency of peak I. This should be 1 ms, but the addition of ear inserts and tubing will normally add a further 1 ms to the latency for a total of 2 ms. There may be delays to this peak

at the commencement of the case but these should not increase during the case. The amplitude of peak I is also measured and providing the stimulation does not change, should not change.

The latencies between peaks I and III and I and V (and therefore III and V) are all used as interpretive parameters. Because the peaks occur in a serial fashion for any given delay between peaks I and III, there should be the same delay between peaks I and V and no further delay added between peaks III and V. Although peak V is most easily identified in the contralateral recording (Ac-Cz), once it is identified there, it is usually identifiable ipsilaterally (Ai-Cz). This makes the latency identification relatively easy. If the peaks are identified at baseline, most modern IOM software will be able to track automatically the latencies throughout a case and alert the user when a threshold change in latency is reached. Similarly the amplitudes of peaks I, III, and V can also be tracked automatically if the peaks are identified appropriately at the commencement of the case [1]. Changes in both absolute latencies as well as changes in interpeak latencies are monitored. Conductive hearing loss or technical issues involving the stimulus not reaching the auditory nerve can cause changes in absolute latencies with no change in interpeak latencies. Intraoperative variability of interpeak latencies suggests sensorineural hearing damage or brainstem injury. A change in the interpeak latency from III to V and an absolute latency change of wave V are most concerning for brainstem ischemia as discussed below.

The same principles apply to the BAEP as to most other evoked potentials in the operating room. A decrease in amplitude tends to indicate that less signal is getting through and an increase in latency indicates a slowing of the conduction velocity [1, 8]. There are a number of caveats to this general statement of course. For instance, a small increase in the conduction delay for the fastest fibers may result in a small increase in latency and a decrease in amplitude. However the amplitude change may be a result of cancellation of some of the signals due to collision.

Typically warning criteria are based upon the latencies of individual peaks and the interpeak latencies. An increase in the latency of peak V is considered the alarm for tumor dissection. There is very little "normal" trial to trial variability in the latencies of the peaks in the BAEP. Changes in the interpeak intervals can therefore be used to help identify the origin of the changes [8].

An isolated increase in the absolute latency of peak III in the absence of a change in peak I will lead to an increase in the I–III latency. If there is no change in the III–V latency, there will however remain an increase in the absolute latency of peak V. For this reason, it is therefore very important to keep track of not just the absolute latencies but also the interpeak intervals. The question then arises as to whether the absolute or relative latencies are the best parameters to monitor. However, as the brief example illustrates, using one or the other is not the best use of our resources and we do need to keep both in mind. Modern machines, especially if you can use a large monitor, allow for the display of tables of latencies and interpeak latencies (these are useful not just for BAEPs but other potentials). Such tables are, I find, the easiest way to track changes in these latencies and distinguish whether a change in the latency of peak V is solely due to changes in the latency of peak III. An alternative scenario, and one which is not uncommon in the case of large posterior fossa tumors, especially in the pediatric population, is that there is a global increase in the latencies. This is manifested as an increase in both the I–III latency and the III–V latency. Consequently both peaks III and V are delayed, and the I–V interpeak latency is also increased. In these situations, the only change that might reach a critical level may be the absolute latency of peak V. However, it is wrong to therefore assume that there is a focal site of damage/injury along the III–V pathway. More likely there is a global change going on, possibly related to changes in blood flow or retraction/compression.

Amplitude decreases are likely to be nonconsecutive in nature, meaning that a 25 % change in peak I amplitude will not give the same change in peaks III and V. Monitoring the amplitude of all of the peaks is therefore still required and any change of more than 25 % should be reported and discussed with the rest of the surgical team.

Changes greater than 50 % are worrisome. However complete absence of peak V has been reported in some individuals who do not experience hearing loss upon awakening, although some authors believe that they may be at higher risk of hearing loss subsequently.

If peak I is absent, then all subsequent peaks will be absent. For this peripheral peak I use the more usual 10 % change in latency and 50 % decrease in amplitude criteria if the surgery is around this nerve. If brainstem function is mostly at risk, data trends not yet reaching significance should always be discussed with the surgical team.

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Electroencephalography

10

Lucy R. Sullivan and Scott Francis Davis

Introduction

The electroencephalogram (EEG) is a graphic display of the spontaneous electrical activity of the cerebral cortex. The EEG represents the output of a differential amplifier whose inputs are two distinct recording locations from the scalp (Fig. 10.1). Continuous EEG recordings are used clinically to diagnosis brain pathology, specifically seizures. Intraoperatively, EEG is used to monitor cerebral perfusion and depth of anesthesia. Cortical SSEPs, discussed in another chapter, are brief averaged EEG epochs recorded following peripheral stimulation.

Discovery of EEG

Hans Berger, a German psychiatrist, was the first to record EEG in humans (Fig. 10.2). Berger initially used a string galvanometer originally designed to record electrocardiograms. The initial recordings were from patients with open craniotomies allowing the needle electrodes Berger used to be place only a few millimeters from the surface of the brain. The first recording through an intact human skull was performed on Berger's son. Berger's first EEG paper titled "Electrokephalogram des Menschen" ("On the Electroencephalogram of Man") was published in 1929 [1]. Berger's reports were met with skepticism mainly due to the seemingly unexplainable slow oscillations (like alpha waves) having durations of about 100 ms. Scientists were expecting the generator of the signal to be single neuronal action potentials with durations of 1–2 ms. In 1935, prominent English physiologists Adrian and Mathews endorsed Berger's work [2], and by 1936 there were six EEG laboratories in the USA [3].

By the 1950s, EEG was well established and the use of intracranial EEG known as electrocorticography (ECoG) was being pioneered by Wilder Penfield and Herbert Jasper to identify epileptogenic foci during epilepsy surgery [4]. ECoG is still used today to map the cortical surface for tumor resection and epilepsy surgery. Conventional EEG is also used in the OR for any procedure where there is a risk of cerebral ischemia and as a means of determining anesthetic depth.

Waveform Generators/Dipoles

Postsynaptic potentials, having longer duration than the action potential, contribute to the EEG waveform [5]. As discussed in another chapter,

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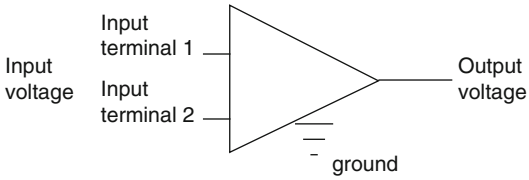

Fig. 10.1 Schematic of a differential amplifier used for EEG recording. The output of a differential amplifier is the difference between the two inputs

Fig. 10.2 Hans Berger (1873–1941) recorded the first human electroencephalogram

postsynaptic potentials are either excitatory (EPSPs) or inhibitory (IPSPs) (Fig. 10.3). The EEG waveform is generated from the complex summation and integration of IPSPs and EPSPs arising from thousands of neighboring cortical neurons [6]. Pyramidal cells, mainly from layers III or V, are the major contributor of these synaptic potentials, which is owed to their spatial

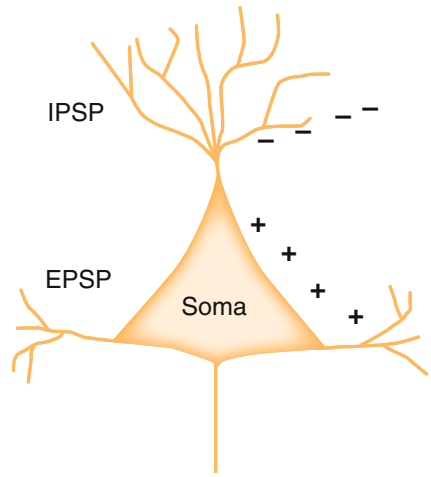

Fig. 10.3 Schematic of a neuron and the influences of postsynaptic potentials. *EPSP* excitatory postsynaptic potential, *IPSP* inhibitory postsynaptic potential

organization within the cortex (Fig. 10.4). Being linearly arranged, these neurons have an open electrical field and produce a dipole (discussed below). The ability to record EEG depends on the synchronization of the cortical neurons. This synchronization is achieved because of the inputs from subcortical structures such as the thalamus.

Neuronal potentials have a negative and a positive field called a dipole. When the discharge is generated at the top of the cortex, it creates a radially (vertically) oriented dipole with a maximum negativity just above the source with a positive field either deep within the hemisphere or in the opposite hemisphere, depending on the orientation of the neuronal field (Fig. 10.5, panel a). When the discharge is generated in a sulcus of the cortex, it creates tangentially (horizontally) oriented dipoles with the fields of maximum negativity and positivity being displayed in an anterior/posterior or medial/lateral orientation (Fig. 10.5, panel b).

10–20 System and Electrode Nomenclature

The International 10–20 System of electrode placement was developed in 1958 as the standard placement of scalp electrodes [7].

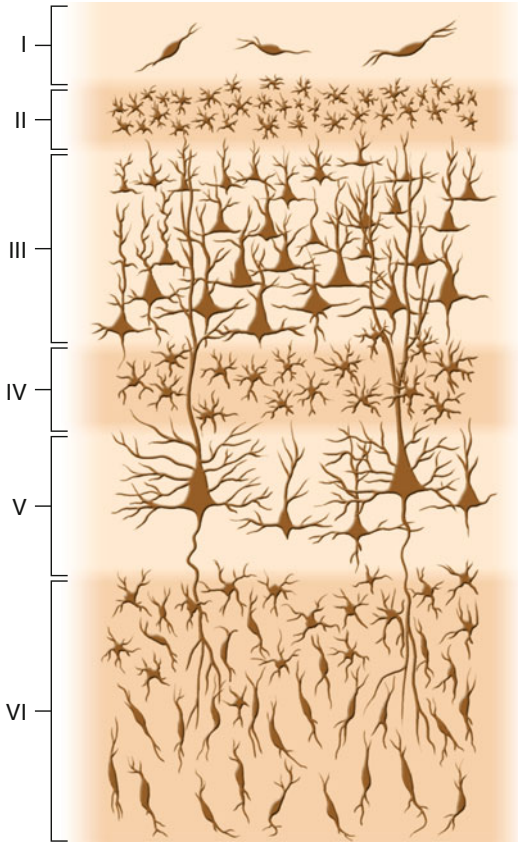

Fig. 10.4 Layers of the cerebral cortex

Anatomical landmarks on the skull are used as reference points for the measurement. The four anatomical landmarks are the nasion, the indentation between the forehead and the nose; the inion, the midline bump or ridge on the back of the skull; and the preauricular points, the indentations just above the cartilage (tragus) on the left and right ears (Fig. 10.6). Electrode designations act as binomial coordinates with the first coordinate of the designation indicating the anterior/posterior position and the second coordinate indicating the medial/lateral position. The anterior/posterior coordinates correlate with brain landmarks such as lobes or sulci. The most common designations used for intraoperative monitoring are shown in Table 10.1.

The medial/lateral electrode positioning has a numerical designation. By convention, electrodes to the right of midline are designated with even numbers and to the left with odd numbers. Electrodes on the midline are designated as "z" because they correspond to an imaginary "z line" that runs along the longitudinal fissure. The numbers increase further from midline.

In 2006, the American Clinical Neurophysiology Society (ACNS) recommended electrode nomenclature using the 10–10 system (Fig. 10.7). T3 and T4 are designated at T7 and T8. T5 and T6 are designated as P7 and P8. The measurements to determine these electrode sites are exactly the same as the International 10–20 System [8].

Electrodes

Various electrode types can be attached to the scalp for the purposes of recording EEG. In a clinical setting, 4–10 mm metal disk or cup electrodes are most frequently used. These may be gold plated, silver, or silver–silver chloride. An electrolyte or conductive gel is placed between the electrode and the scalp to lower impedance and increase the quality of the signal. The electrode is secured with an adhesive such as collodion or paste. Desirable electrode impedances are under 5 kΩ. For intraoperative EEG, stainless steel subdermal needles are more commonly used. These can be quickly and safely inserted just under the scalp and provide excellent quality recordings. Electrode removal is likewise quick and clean!

Montages

A montage is a systematic and logical combination of multiple pairs of electrodes that are used for electrophysiological recording. An acceptable montage for EEG should compare activity from homologous electrodes between the two hemispheres. For intraoperative monitoring, there are two main types of recording montages: bipolar and referential. Bipolar montages compare active electrode sites adjacent to each other. An example of a bipolar montage used for EEG is the anteroposterior (AP) montage (Table 10.2).

Referential montages compare an active site recording a biologic signal of interest to a common

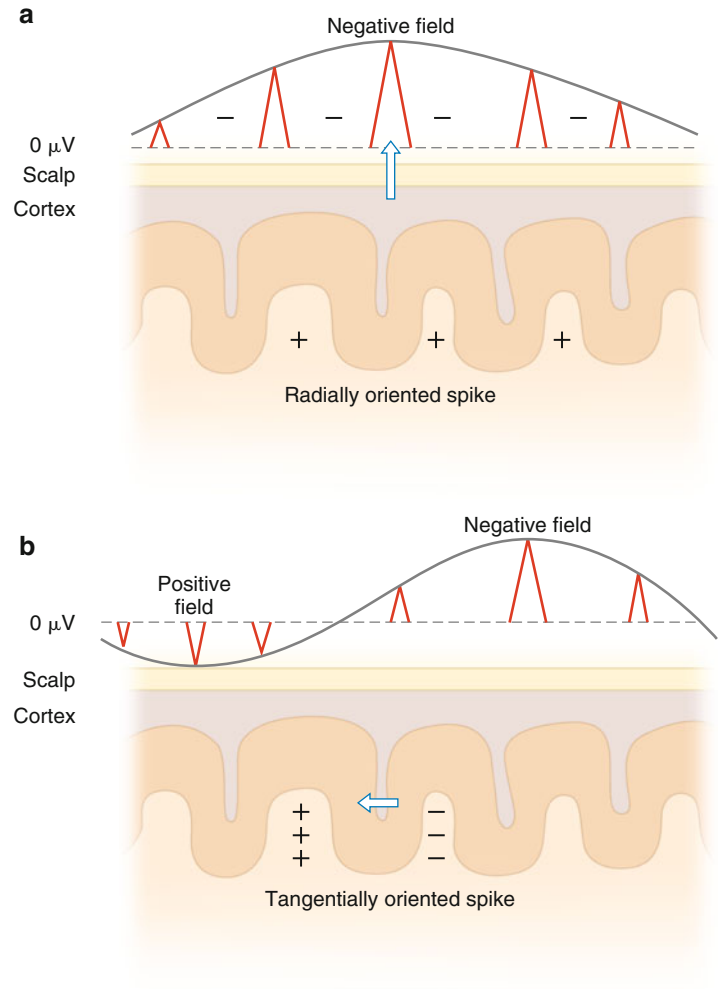

Fig. 10.5 Schematic representation of dipoles in relationship to the scalp surface. Panel **a** depicts a radially oriented discharge arising from the crown of the cortex with a negative field above the source and a positive field within the cortex. Panel **b** depicts a tangentially oriented discharge arising from a sulcus with surface negative and positive fields posterior and anterior to the source

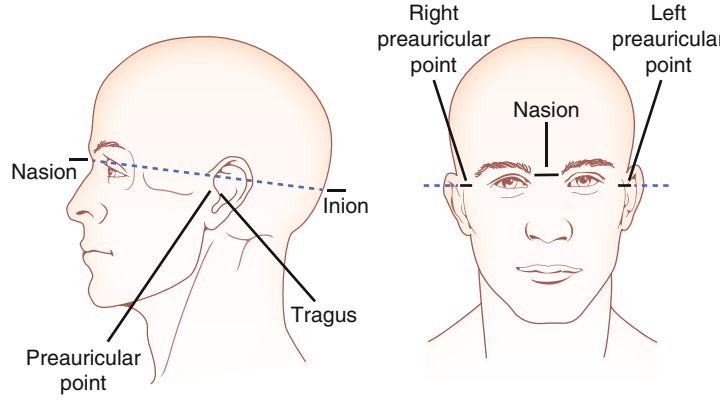

Fig. 10.6 Skull landmarks that are reference points for the International 10–20 System of electrode placement

reference some distance away. Ideally the reference should be inactive, meaning that it does not "see" the biologic signal of interest. Unfortunately it is very difficult to find an inactive reference. Sites commonly used for the reference electrode include earlobes, skin over the mastoid process, the nose, the chin, the Cz electrode, and the base of the neck. An example referential montage is shown in Table 10.3.

A bipolar montage has an advantage of greater specificity than a referential montage since the electrode pair lies closer together.

Table 10.1 International 10–20 System electrodes most commonly used during intraoperative neurophysiological monitoring

A/P designation	Name	Description of location
Fp	Frontopolar	Over frontal pole of brain
F	Frontal	Over frontal lobe
T	Temporal	Over temporal lobe
C	Central	Along central sulcus
Cp	Central–parietal	Midway between C and P line
P	Parietal	Over parietal lobe
O	Occipital	Over occipital lobe

Table 10.2 Anteroposterior (AP) bipolar montage for recording EEG

Left	Right
Fp1–F3	Fp2–F4
F3–C3	F4–C4
C3–P3	C4–P4
P3–O1	P4–O2
Fp1–F7	Fp2–F8
F7–T3	F8–T4
T3–T5	T4–T6
T5–O1	T6–O2

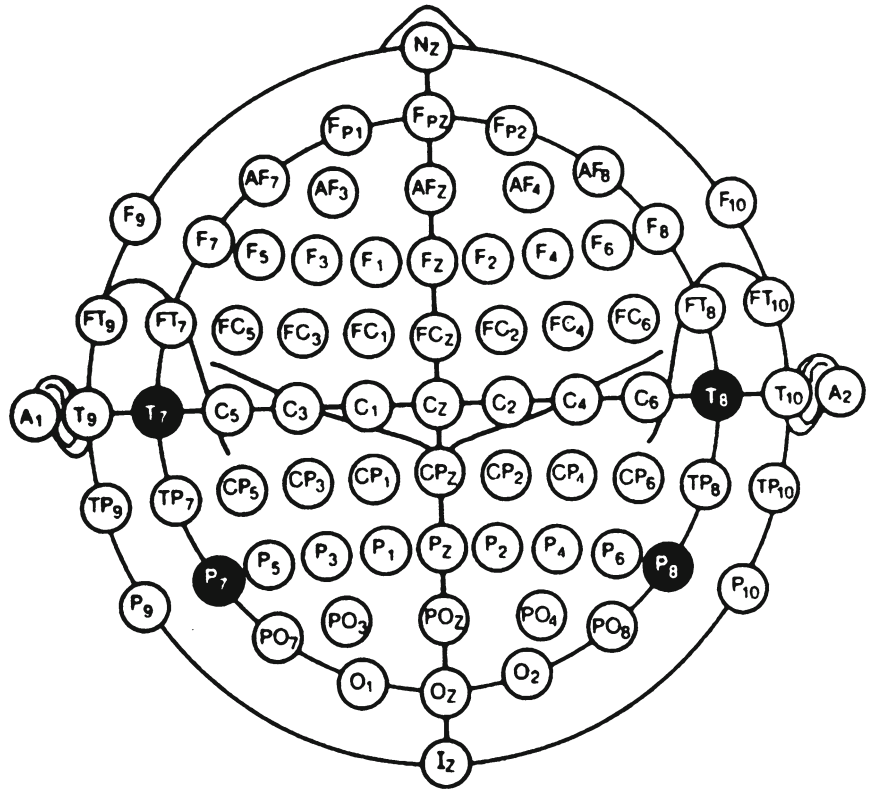

Fig. 10.7 Nomenclature for the 10–10 system

Table 10.3 Referential montage using the ipsilateral earlobes as the reference

Left	Right
Fp1–A1	Fp2–A2
F3–A1	F4–A2
C3–A1	C4–A2
P3–A1	P4–A2
O1–A1	O2–A2
F7–A1	F8–A2
T3–A1	T4–A2
T5–A1	T6–A2

Referential montages may provide more sensitivity but are less specific. The need to localize a change would make a bipolar recording preferred. If sufficient number of channels is used, these montages can also be quite sensitive.

The number of channels needed is dependent on the purpose of the EEG. The more channels recorded, the greater both the sensitivity and specificity of the EEG will be. For intraoperative monitoring, amplifier space and time are factors that may limit the number of recorded channels. Most IOM practitioners will use a minimum of eight channels for intraoperative EEG.

Recording Parameters

Filters

Filters can be used to accentuate EEG activity but when used improperly can greatly attenuate EEG waveforms. Filters remove waves according to rigid mathematical rules and cannot discriminate EEG waveforms from artifact. Filters are discussed more completely in another chapter of this book. The use of analog filters changes the raw data prior to digitization and display and cannot be undone. In addition to the loss of data, aggressive use of analog filters may cause phase shifts in the data. These artificial alterations in the raw EEG data are best avoided with careful use of analog filters. When selecting analog filters for any bioelectric recording, it is important to know the frequency characteristics of the signal of interest. For intraoperative EEG, we generally desire a pass band between 0.5 and 70 Hz. These filter settings will allow the desired signal while minimizing high-frequency artifact. A notch filter may be used to eliminate 60-cycle noise as most of our EEG signal will fall at frequencies much lower than this. Unlike evoked potential recordings, where ringing artifact may occur with the use of a notch filter, the EEG is a passive recording and does not introduce the risk of a ringing artifact with notch filter use.

Display Parameters

Historically analog EEG was performed with a roll of paper moving under a series of pens (one for each channel) that would deflect proportionally to the recorded voltage output of the amplifier. The paper speed could be adjusted to change the display property of the EEG with slower paper speeds used to distinguish asymmetric slowing. By convention, the EEG time base is defined as the paper speed in millimeters or centimeters per second. Some modern intraoperative monitoring equipment, however, uses the same convention for EEG display as for evoked potentials, which is milliseconds/division. A division is generally one centimeter for most equipment and there are usually ten divisions in the test window. A good starting point for intraoperative EEG is 1,000 ms/div which gives a 10 s sample of data in the window. The display sensitivity for voltage should initially be set near 70 μV/division. These parameters can be adjusted out of clinical necessity or personal preference.

Normal EEG Patterns

Analysis of EEG waveforms includes voltage, frequency, morphology, and topography.

EEG is a mixture of frequencies that vary greatly during infancy and childhood and again in the elderly. Normal EEG has an anteroposterior gradient characterized anteriorly by waves of lower voltage and higher frequency and posteriorly by waves of higher voltage and lower frequency.

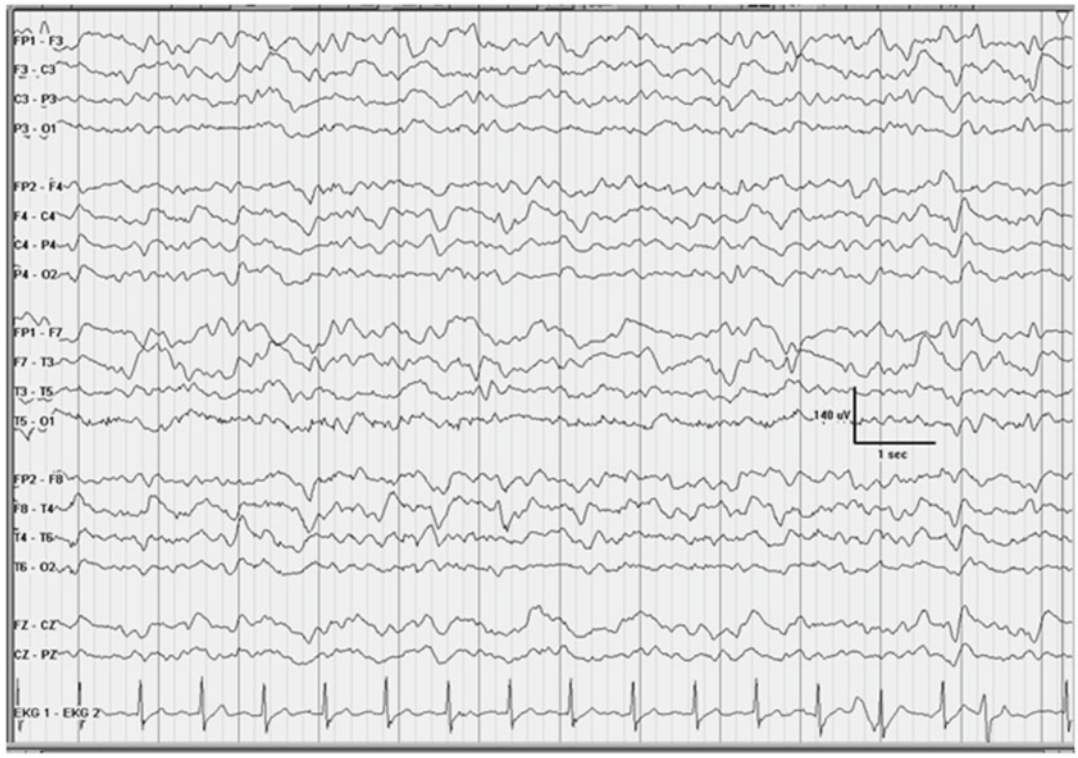

Fig. 10.8 Diffuse underlying delta activity with faster theta frequencies superimposed. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

The five (with the introduction of gamma) EEG frequencies are:

- Delta: less than 4 Hz
- Theta: 4–7 Hz
- Alpha: 8–13 Hz
- Beta: 13–35 Hz
- Gamma: 35 Hz and above

Delta activity is normal in preterm neonates and in deep sleep (Fig. 10.8). Persistent delta activity without theta or alpha activity is abnormal if seen during wakefulness at any age [9]. Theta activity is enhanced by drowsiness and sleep (Fig. 10.9). There is great individual variation in the waveform, frequency, and amplitude of frontal and frontocentral theta seen in children and adults. The normal posterior dominant rhythm in adults is in the alpha frequency and is 8.5–11 Hz. The posterior dominant alpha rhythm is seen bilaterally over the posterior head region and attenuates with eye opening (Fig. 10.10). Beta activity increases with drowsiness, light sleep, and mental activation (Fig. 10.11). Sedative, hypnotic, and anxiolytic drugs, such as benzodiazepines and barbiturates, are potent activators of beta especially in the frontal and central regions. Gamma activity may be associated with conscious perception and attention processing [10] (Fig. 10.12).

Abnormal EEG Patterns

Abnormal EEG patterns are nonspecific for etiology. Abnormal activity can be focal, bilaterally diffuse, and unilateral or lateralized.

Abnormal EEG can be:

1. Slowing of the background rhythm
2. Appearance of slow waves—arrhythmic delta activity (polymorphic delta) or intermittent rhythmic delta (monomorphic delta with a stereotyped waveform)

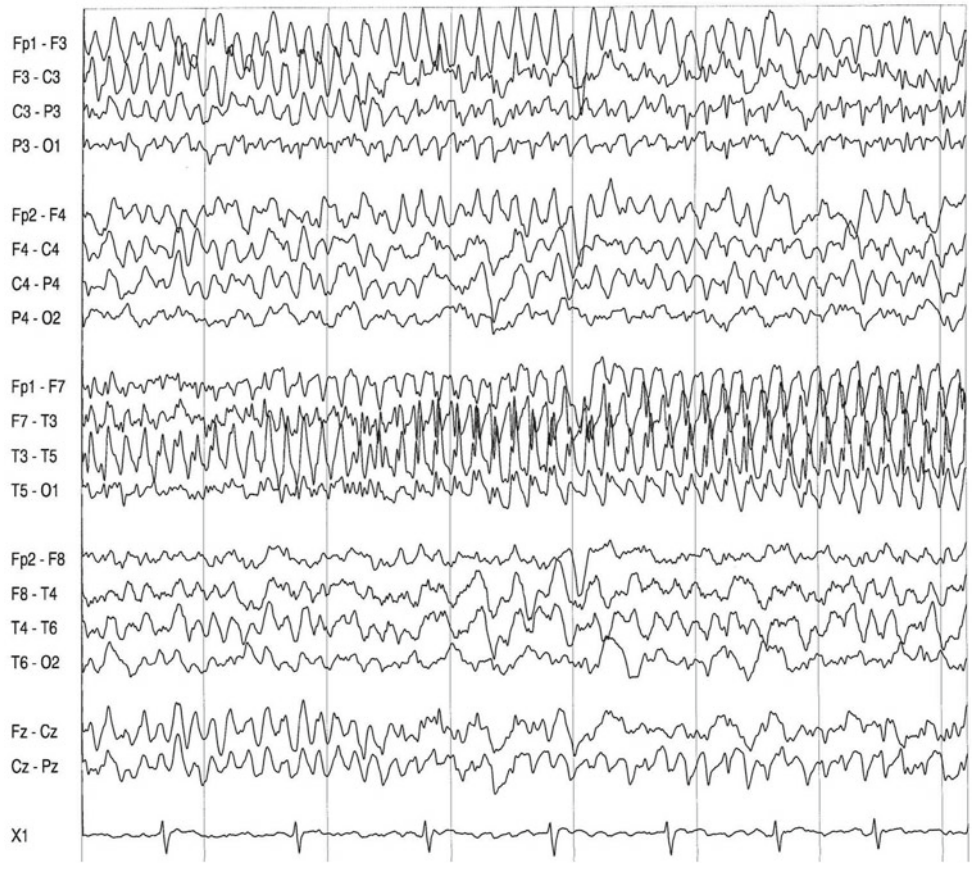

Fig. 10.9 Rhythmic theta activity seen in the left hemisphere signaling the onset of a seizure. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

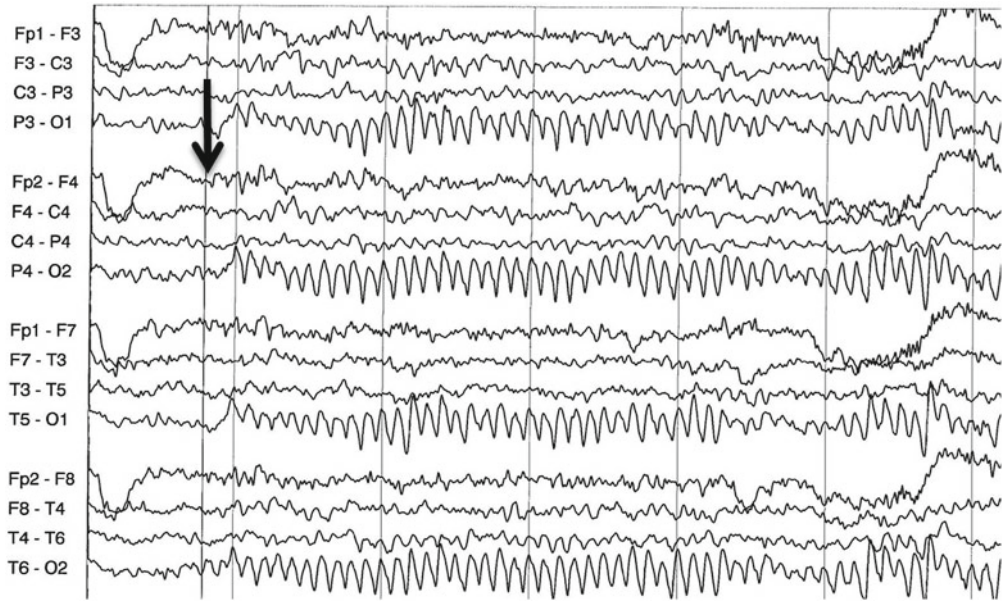

Fig. 10.10 Alpha activity attenuates or blocks (*closed arrow*) with eye opening. Alpha activity returns with eye closure (*open arrow*). Time between *solid vertical lines* = 1 s. Sensitivity = 7 μV/mm. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

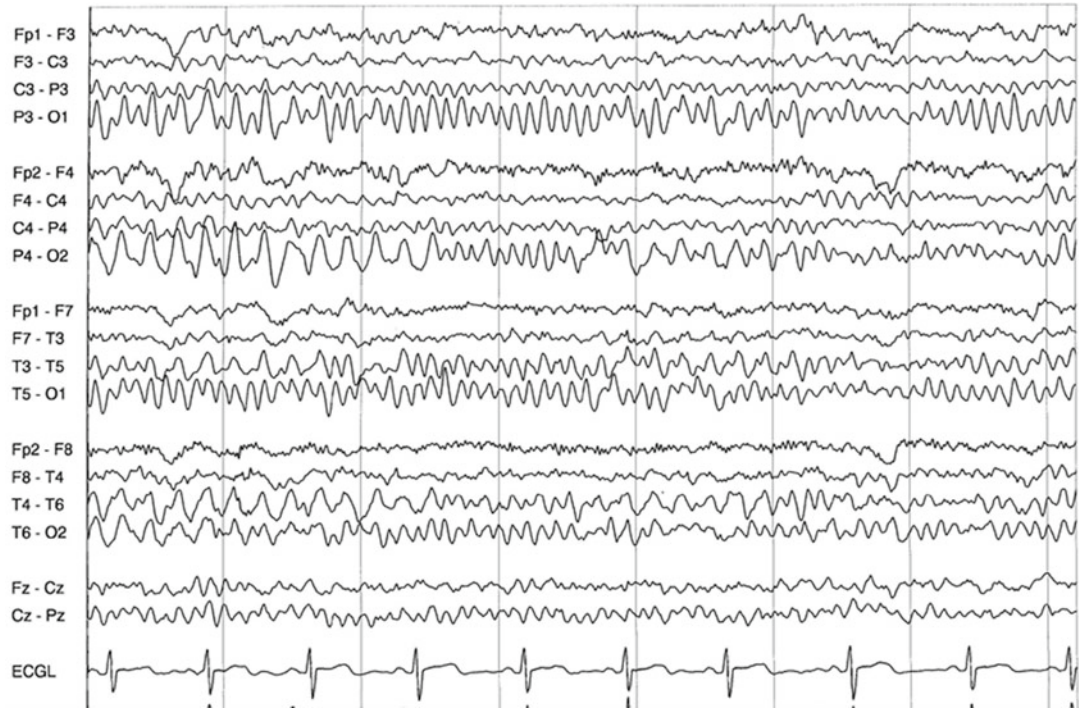

Fig. 10.11 Bifrontal beta activity; *oval* indicates an example. Time between *solid vertical lines* = 1 s. Sensitivity = 10 μV/mm. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

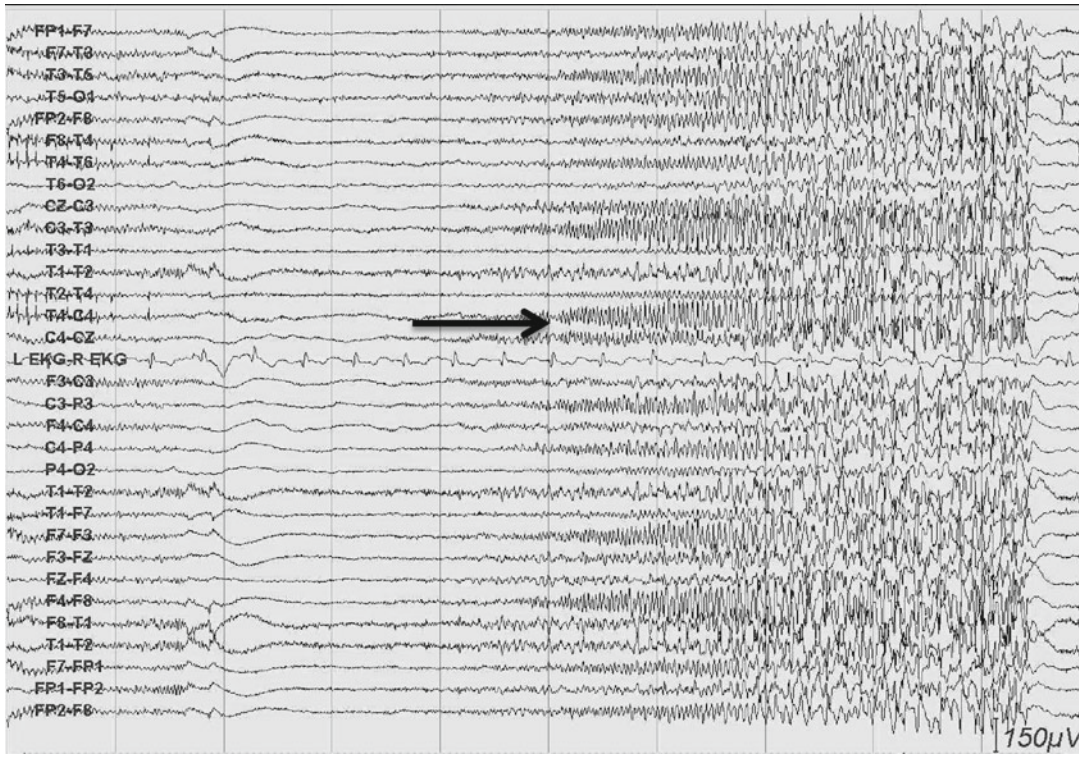

Fig. 10.12 Gamma activity seen at the onset of a seizure (*arrow*). Time between *solid vertical lines* = 1 s. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

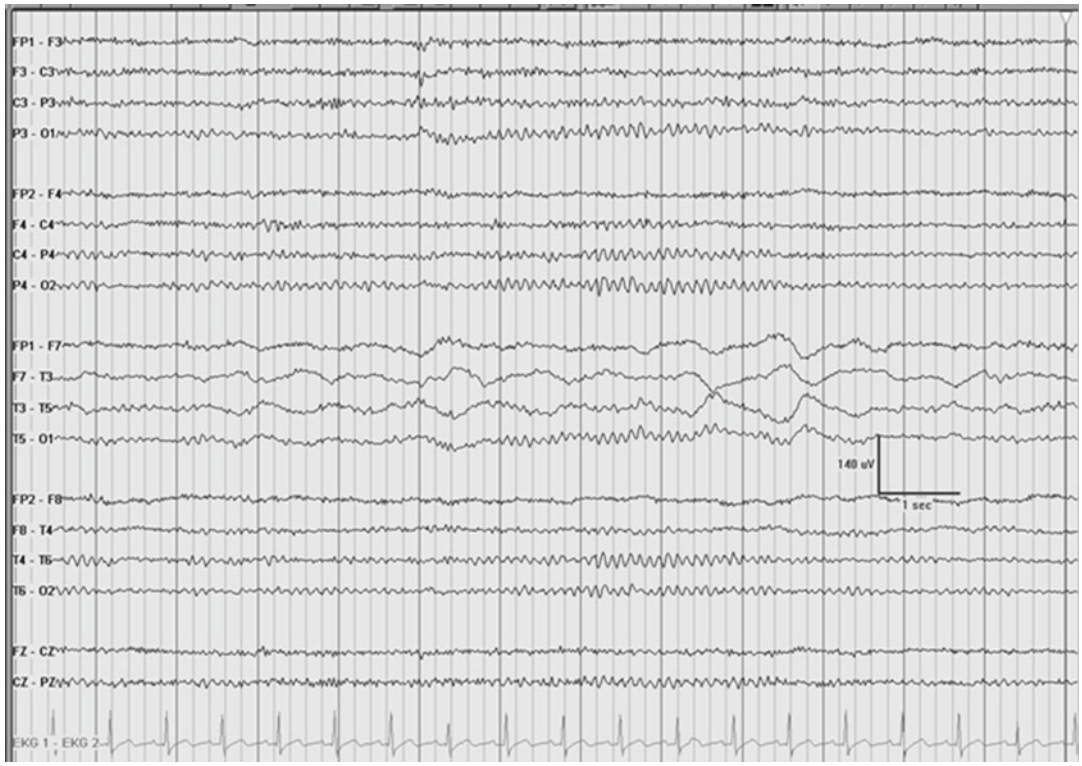

Fig. 10.13 Focal left temporal delta. Normal alpha rhythm is seen in both left and right occipital regions. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

3. Paroxysmal activity—discharges of abrupt onset and sudden termination that are clearly distinguishable from the ongoing background
4. Specific patterns—burst suppression, periodic lateralized epileptiform discharges, triphasic waves, and generalized periodic epileptiform discharges

Focal EEG abnormalities provide electrographic evidence of localized, abnormal cerebral function that is nonspecific for the etiology and may be seen with many different underlying lesions of the brain (Fig. 10.13). Some of the causes of focal EEG abnormalities include head trauma, tumor, stroke, intracranial hemorrhage, abscess, and herpes encephalitis.

Diffuse EEG abnormalities are also etiologically nonspecific. Diffuse slowing may have various morphologies and occur intermittently or continuously and reflect abnormal cerebral function. Diffuse slowing suggests a bilateral disturbance of cerebral function and represents an encephalopathy that is nonspecific for etiology. The most common causes of diffuse slowing are toxic, metabolic, infectious, or systemic disturbances although severe diffuse lesions affecting the brain can produce diffuse slowing. Traumatic brain injury, coma, post-seizure state, advanced neurodegenerative diseases, ischemia, and even anesthesia can cause diffuse slowing.

Epileptiform discharges are distinctive waves or complexes, distinguished from background activity, and resembling those recorded in a proportion of human subjects suffering from epileptic disorders and in animals rendered epileptic experimentally [11]. Epileptiform patterns include spikes and sharp waves, with or without accompanying slow waves, which occur singly or in bursts (Fig. 10.14). Spikes have a duration of 20–70 ms. Sharp waves have a duration of 70–200 ms. Epileptiform activity does not equate a diagnosis of epilepsy [12].

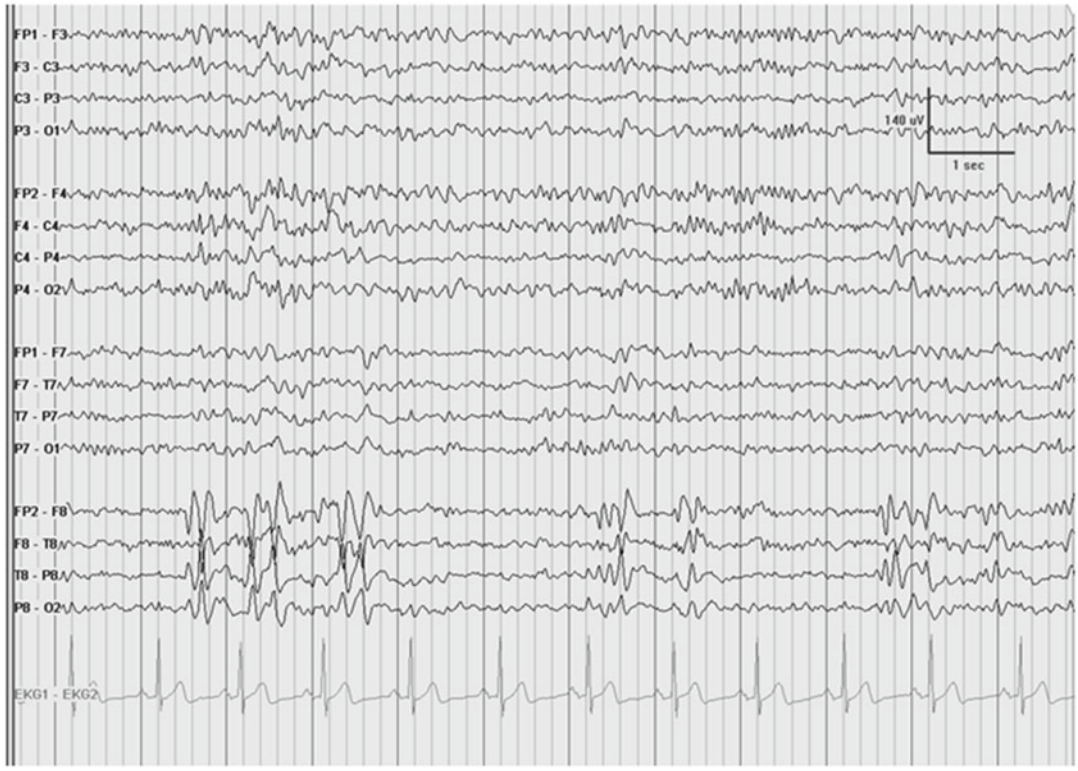

Fig. 10.14 Right temporal sharp waves occurring during sleep. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

Anesthesia Effects

EEG recorded from the anesthetized patient is very different than EEG from the awake patient recorded in the neurology clinic. General anesthesia results in generalized slowing of the EEG pattern and the IOM clinician must be aware of these effects when establishing baseline criteria from which to compare all intraoperative data. While preinduction baselines can illuminate asymmetries in the EEG that will need to be documented, baselines taken during this time are not adequate for monitoring for intraoperative changes. A post-induction baseline is required and is the only baseline that intraoperative data should be compared to.

Burst Suppression

Burst suppression is an EEG pattern seen with pathology or as a result of general anesthesia. It is characterized by periods of low-voltage (nearly isoelectric) activity punctuated with brief bursts of activity (Fig. 10.15). Monitoring EEG for cerebral ischemia is not possible when the EEG is in a burst suppression pattern due to the large periods of electrical silence. For some procedures, a burst suppression pattern is induced intentionally as a mechanism of cerebral protection. The burst suppression pattern is characteristic of a metabolic state that requires less oxygen and therefore less blood. A burst suppression ratio of 1:4 is defined as 1 s of bursting for every 4 s of isoelectricity.

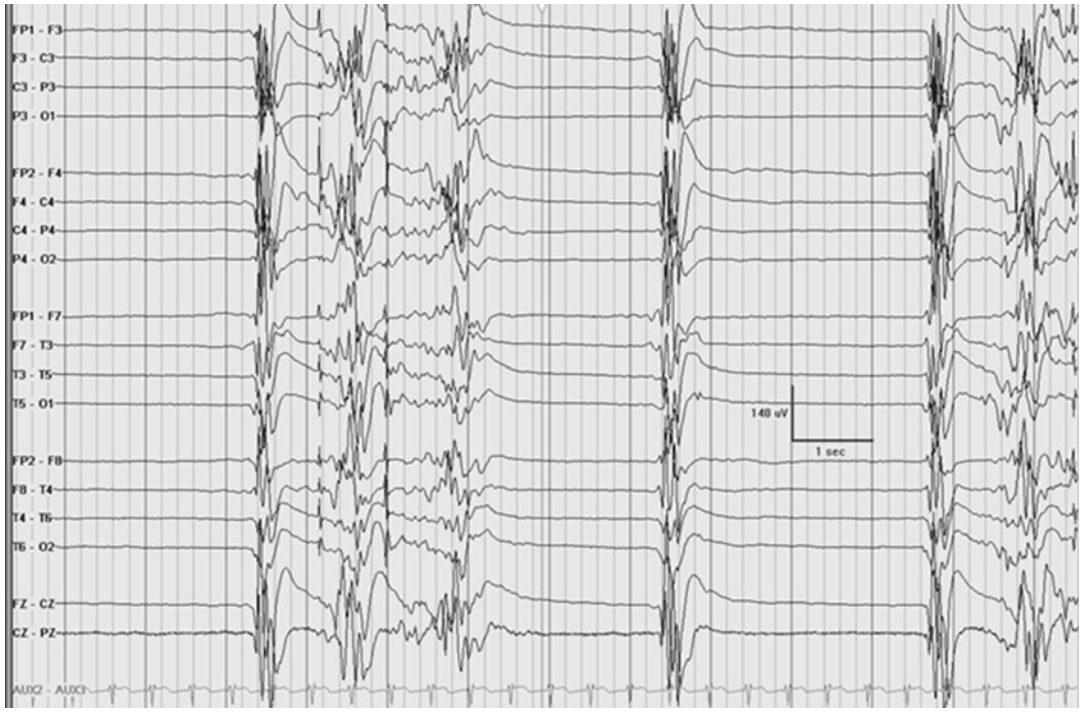

Fig. 10.15 Burst suppression. EEG epoch reprinted with permission of ASET—The Neurodiagnostic Society

This is the ratio demonstrated to be the most cerebroprotective. The IOM clinician is often called upon to monitor for adequate burst suppression and to work with the anesthesia team to deliver more drugs if cerebral activity begins to increase. Barbiturates such as thiopental are most often used to induce burst suppression. Propofol is another agent that is frequently used for this reason. When EEG cannot be a reliable indicator of cerebral ischemia because of the burst suppression pattern, the IOM clinician can rely on the cortically generated SSEP, which is still monitorable.

Use of EEG in IONM

The most common use of EEG during surgery is to monitor the adequacy of cerebral perfusion during procedures that may reduce blood flow to the brain such as carotid endarterectomy. As discussed above, monitoring for adequate burst suppression ratio is indicated for certain procedures such as cerebral aneurysm clipping or coiling. Intracranial EEG may be used to help identify the eloquent cortex and is briefly discussed below.

Intraoperative EEG may also be useful in determining the depth of anesthesia. Commercial devices that apply a proprietary algorithm to a two-channel frontal EEG are used by anesthesiologists to monitor anesthetic depth. This method is less reliable than a multichannel raw EEG used for the same purpose and is marketed to clinical personnel without sufficient EEG experience to interpret the raw data.

Electrocorticography

Intracranial EEG also called electrocorticography is used generally for mapping functional brain areas or defining epileptogenic foci. ECoG recordings from surgical implanted intracranial electrodes have direct contact with the neural tissue (Fig. 10.16). This technique has greater spatial resolution, sensitivity, and overall signal quality when compared to scalp EEG. By eliminating electrical resistors such

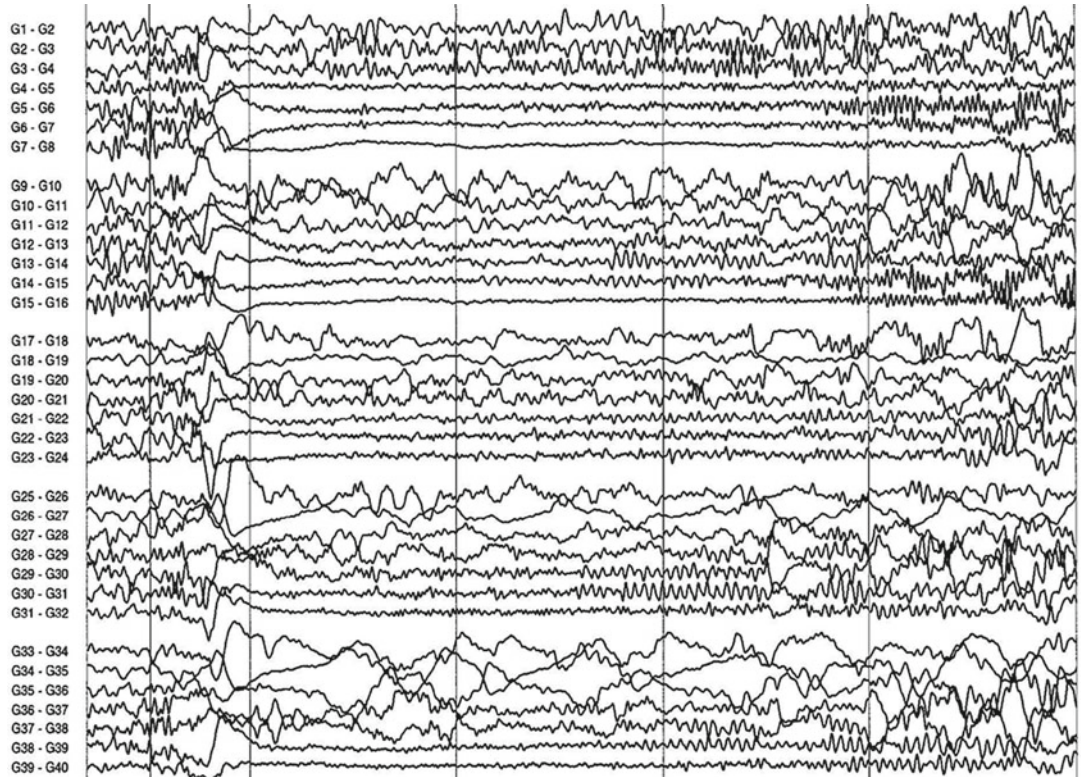

Fig. 10.16 Electrocorticogram (ECoG) recorded from a subdural grid. ECoG epoch reprinted with permission of ASET—The Neurodiagnostic Society

as the dura, skull, and scalp, ECoG allows recording of faster frequencies and elimination of artifacts generated by scalp muscles and eye movements.

Conclusion

The use of EEG whether for diagnostic purposes in the clinic or for monitoring purposes in the operating room has had a huge impact on the lives of patients. Electrophysiological recordings, such as EEG, provide real-time functional information about the patient's nervous system that cannot be achieved with even the best imaging techniques at this time.

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The H-Reflex and F-Response

11

Jeremy Andrew Bamford and Scott Francis Davis

Introduction

Common electrophysiological recording modalities applied in the surgical setting include somatosensory evoked potentials (SSEPs), motor evoked potentials (TcMEPs), and electromyography (EMG). Central function is traditionally monitored with SSEPs and TcMEPs. Spinal nerve and nerve root function can be more easily assessed with EMG. While generally accepted to provide complete spinal cord protection, SSEPs are specific for the dorsal white matter tracts and the vascular territory of the posterior spinal arteries. The TcMEP is specific for monitoring descending white matter pathways of the lateral and anterior columns, but is also distinct in being the only routinely applied modality to monitor the integrity of the spinal gray matter. While useful in detecting gross changes in motor function as a result of spinal cord injury, TcMEPs do not monitor more complex spinal circuits including multisegmental, interneuronal, and propriospinal circuitry responsible for the control of voluntary movement. Furthermore, TcMEP monitoring has some contraindications and typically causes considerable patient movement and the risk of bite injury. Two other modalities, the Hoffmann reflex (H-reflex) and the F-response, have been proposed as valuable adjuncts to SSEPs and TcMEPs for monitoring spinal cord integrity during neurosurgical spine procedures [1].

The eponymously named Hoffmann reflex (H-reflex) is an electrical analogue of the tendon tap reflex. The H-reflex was first described in the early 1900s by Piper [2] and then further elaborated by Hoffmann [3], who described a long-latency muscular contraction in the triceps surae muscle in response to submaximal electrical stimulation of the posterior tibial nerve. The reflex was further studied in a series of papers in the 1950s by Magladery and colleagues, who first named this response for Paul Hoffman [4]. The H-reflex is still used in laboratory settings to assess neuronal organization and to interrogate the plasticity of spinal cord circuitry and in clinical practice to assess spinal reflexes, peripheral conduction velocity, and spasticity [5, 6].

Physiology of the Stretch- and H-Reflex

The H-reflex is an electrically evoked response that operates via the same neuronal circuitry as stretch reflexes. In order to understand H-reflexes,

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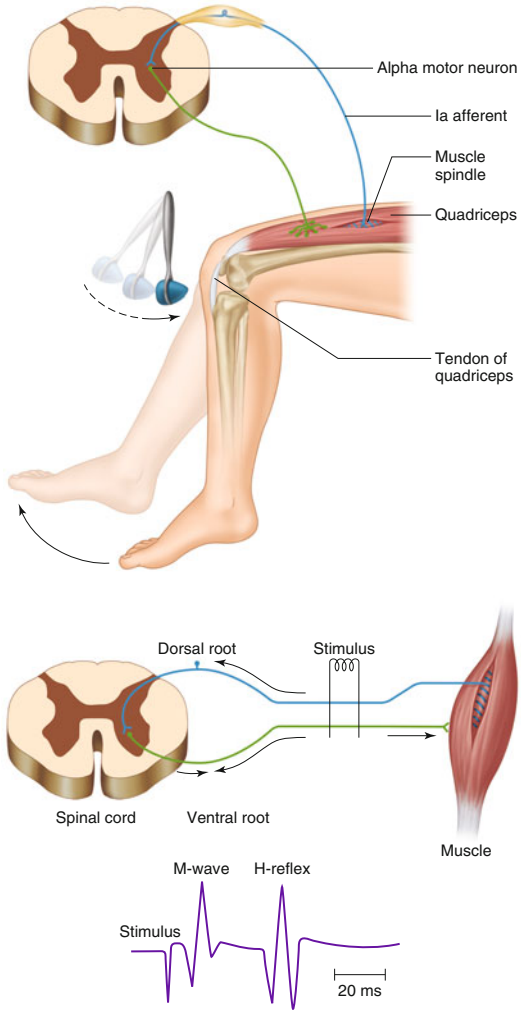

Fig. 11.1 The monosynaptic stretch reflex. (**a**) In response to rapid stretch sensory Ia afferents activate alpha motoneurons in the ventral horns of the spinal cord resulting in a delayed contraction of the muscle that was stretched. Clinicians make use of this response to test spinal cord reflexes. (**b**) The same pathways can be assessed intraoperatively using the H-reflex. A peripheral nerve is electrically stimulated, producing two responses that can be recorded with EMG. An early response, known as the M-wave, is elicited by direct activation of the muscle via motor axons. A later response, the H-reflex, is the result of activation of sensory Ia afferents, similar to what occurs when the muscle is stretched

it is best to review the basic physiology and anatomy of the standard monosynaptic stretch reflex (Fig. 11.1a). Monosynaptic stretch reflexes, sometimes referred to as deep tendon reflexes, are evoked by clinicians during standard reflex testing and can be generated at multiple points on the body by performing a tendon tap with a small rubber mallet. When the muscle is stretched via a tendon tap stretch-responsive sensory neurons termed Ia afferents are activated. The cell bodies of these Ia afferent neurons are located in the dorsal root ganglion. The central process of these neurons sends a collateral that terminates on alpha motor neurons in the ventral horn of the spinal cord gray matter. This synapse evokes a delayed contraction in the muscle from which the tendon reflex was initiated. The presence of a delayed muscular contraction in response to tendon tap as well as the latency of the muscular response can be evaluated in order to confirm the integrity of spinal cord reflexes. From a gross clinical perspective, the reflex is considered normal if an involuntary muscle contraction is observed after a slight delay following the tendon tap. The noticeable delay, or latency of the response, is a result of the fact that the signal must travel along sensory axons towards the spinal cord, synapse in the spinal cord, and then travel along motor axons back to the muscle before finally evoking a muscular response.

Electrically Evoked Responses

Unlike the stretch reflex that is detected by visual observation, EMG is used to record the M-wave, H-reflex, and F-response. In EMG testing, muscle contractions are recorded as compound muscle action potentials (CMAPs). Electrophysiological recordings afford the clinical scientist the opportunity to make precise measurements of latency, amplitude, and morphology (Fig. 11.1b).

Two physiological differences distinguish the H-reflex from the stretch reflex: (1) the H-reflex is evoked by electrical stimulation of a mixed motor and sensory nerve rather than by muscular stretch and (2) the H-reflex is activated proximal to the muscle and avoids entirely the muscle spindle fibers which, along with gamma motor neurons, play a role in modulating stretch-reflex gain. These factors make the H-reflex well suited to assessing spinal cord excitability [7].

The H-Reflex

Electrical activation of a mixed peripheral nerve creates an action potential that propagates in both directions along both sensory and motor axons (i.e., both ortho- and antidromically in afferent and efferent axons). The stimulation threshold for the H-reflex is typically low, and the reflex response is characterized by consistent latency between trials and simple morphology, leading to the conclusion that the reflex is mediated by large-diameter, monosynaptic Ia afferent fibers [5]. Despite this, there is some evidence for oligosynaptic components to the H-reflex response [6].

In humans, the CMAP response evoked by the lowest intensity stimulation is likely to be the H-reflex. The stimulus intensity where the H-reflex is first recorded is near or below the motor threshold, and therefore, an orthodromic motor response (M-wave) may not be recorded.

The H-reflex response is most like the muscle stretch reflex as it is evoked by the same process whereby a signal travels orthodromically along Ia sensory afferents towards the spinal cord, crosses the synapse onto alpha motor neurons, and then travels orthodromically along efferent motor axons to the muscle where it evokes a delayed muscular contraction [5]. Because of this similar route, it shares a similar characteristic delay with the stretch reflex. H-reflexes evoked at the popliteal fossa and recorded at the *soleus* muscle typically have a latency of ~30 ms, while those evoked at the cubital fossa and recorded at the *flexor carpi radialis* muscle have a latency of ~18 ms [8]. As with the stretch response, this delay is due to the longer route that this signal must take.

The M-Wave

As stimulation intensity is gradually increased, a shorter latency CMAP begins to appear in the recording. This response is termed the M-wave and is activated not through a reflex circuit but via the direct orthodromic transmission of an action potential along the motor axon to the neuromuscular junction. The stimulus intensity where the M-wave is first recorded is the termed the motor threshold. The M-wave response has the shortest latency because it is the simplest physiologically, being the result of the direct activation of the motor axon and subsequent transmission of an action potential to the neuromuscular junction, producing a contraction of the postsynaptic muscle. As stimulus intensity increases further, the H-reflex will peak in amplitude and then begin to decline as the M-wave increases. Near supramaximal stimulation intensities, the M-wave dominates the recording as its amplitude peaks and the H-reflex disappears altogether.

The F-Response

By the time stimulus intensity becomes supramaximal, a third CMAP response appears on the EMG recording with a similar latency to the H-reflex. Termed the F-response, this response is not a reflex but is generated by an action potential that travels first antidromically and then orthodromically along motor axons. As just explained, the initial orthodromic action potential generated by electrical stimulation will generate a short-latency response, the M-wave. However, the same motor axons will also generate antidromic action potentials that travel towards the spinal cord along the same axons. When the antidromic action potential reaches the motor neuronal pools, the majority of these action potentials will be abolished. However, some of these signals will survive to depolarize the cell body causing an orthodromic action potential to form and travel back down the same motor axons. This "backfiring" of the motor neuron results in a CMAP response in the EMG recording. The population of motor units recruited to produce an F-response will vary from trial to trial yielding variable amplitude, latency, and morphology. This is one way in which the F-response can be distinguished from the H-reflex [9].

Ordered Responses Explained

The H-reflex, M-wave, and F-response are recruited in an ordered manner by electrical stimulation of

increasing intensity. This occurs because the excitability of axons when evoked by electrical current is directly related to their diameter and input resistance; the largest axons will be recruited by the lowest stimulus intensity [10]. The largest diameter axons in a mixed peripheral nerve are the Ia afferent axons responsible for carrying the sensory action potential which initiates the H-reflex. The second largest group of axons are those of the alpha motor neurons, especially those that innervate larger, fast-twitch fatigable motor units in skeletal muscle. There is some overlap in the diameters of these axons, which explains why there is also some overlap in the intensities at which the M-wave and H-reflex are recorded. Nevertheless, the H-reflex is typically first noted at stimulus intensities that are subthreshold for the M-wave.

Advantages of the H-Reflex

Because H-reflexes are single-sweep and do not require averaging they offer a real-time test, similar in this respect to TcMEPs. They are also like TcMEPs in that they involve spinal cord circuitry in the gray matter; however, unlike TcMEPs they can be run without having to pause or interrupt the surgery as they produce little or no detectable movement. Furthermore, they have been shown to be stable with anesthetic regimens commonly employed to allow intraoperative monitoring [11].

Perhaps the greatest physiological advantage of H-reflexes is that they can be used to assess not just the nerve roots through which the afferent and efferent signal travels but complex suprasegmental, propriospinal, and interneuronal circuitry that affects the reflex arc both pre- and postsynaptically [6]. When evoked by stimulation of the posterior tibial nerve at the popliteal fossa, or the median nerve at the cubital fossa, H-reflexes can be minimally understood to be providing information about the integrity of S1 and C6/C7 nerves and nerve roots, respectively. However, the potential advantage of H-reflex monitoring is that it may provide a way of monitoring the integrity of a much larger network of suprasegmental spinal cord circuitry. Leppanen has speculated that the loss of H-reflexes following spinal cord trauma may have to do with uncoupling of the central pattern generator in humans and the disruption of inputs onto segmental afferents, yielding a change in reflex gain [8]. Although this is an intriguing hypothesis, it is difficult to be certain about the specific mechanisms of H-reflex suppression in humans following spinal cord trauma.

Two reports using H-reflexes in the operating room have described H-reflexes as being remarkably sensitive to intraoperative events. Standard surgical maneuvers such as hammering with a mallet, distraction, and derotation of the spine resulted in transient decreases in H-reflex amplitude [12, 13]. This decrease in H-reflex amplitude was repeatedly observed across multiple procedures and was correlated with stressful spinal manipulations and perturbances of the spinal cord. The authors of this chapter have observed similar decreases in H-reflex amplitude correlated with spinal corrections or EMG bursts observed during posterior decompressions (Fig. 11.2).

Practical Considerations

Anesthesia

As with other intraoperative modalities, H-reflex and F-response data can be compromised by anesthetic regimens that are not optimized to provide the best environment for achieving valid neurophysiological results. Critically, H-reflexes and F-responses rely upon accurate recordings of muscular contraction via EMG. As such, they are strongly affected by paralytics applied during surgery. Neuromuscular blocking agents will diminish or even abolish the CMAP responses evoked as H-reflexes or F-responses. Interpretation of H-reflexes and F-responses should take into account the degree of neuromuscular blockade.

H-reflexes are modified by complex multisegmental, propriospinal, and interneuronal spinal networks [6]. Commonly applied anesthetics can alter the excitability of these networks, potentially yielding invalid results. H-reflex and F-response amplitudes are diminished significantly by the

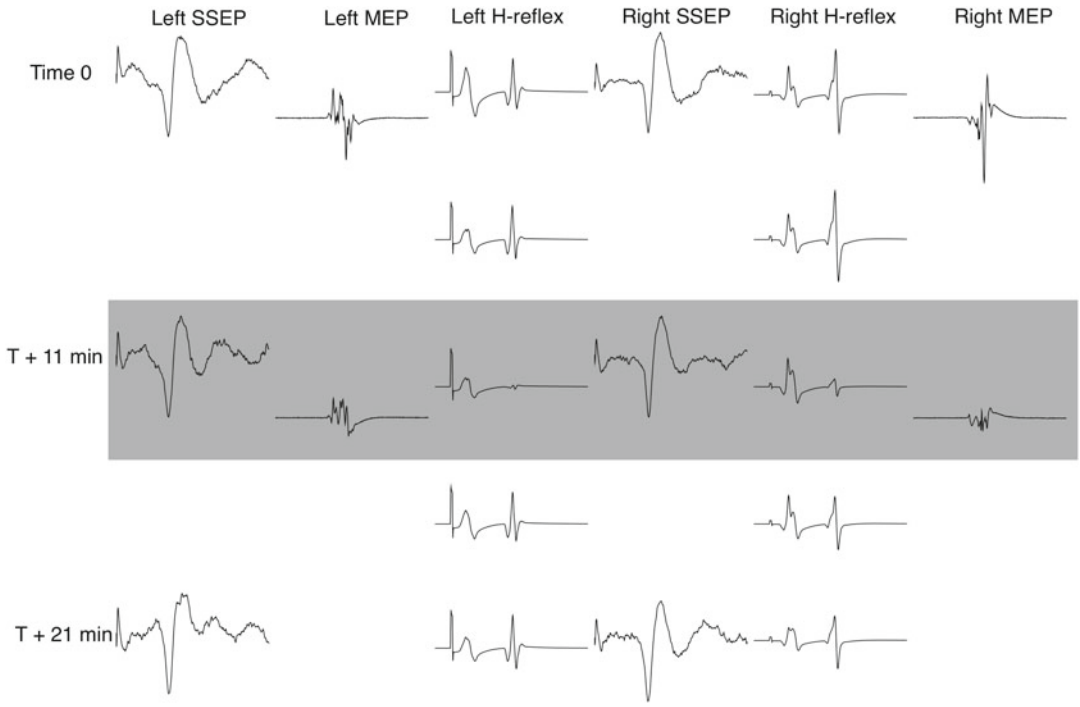

Fig. 11.2 The H-reflex is sensitive to spinal irritation. Displayed signals were gleaned during a complex scoliosis correction in an 18-year-old male. SSEP and H-reflex tests were gathered at regular intervals, while the TcMEP was run as often as practical, in communication with the surgical team. Pictured signals include bilateral cortical SSEPs evoked from the posterior tibial nerve, bilateral H-reflexes recorded at the *soleus* muscle, and bilateral TcMEPs recorded at the *abductor hallucis* muscle. During osteotomy, a large EMG burst (not shown) was observed across multiple lower limb muscles bilaterally in response to a distinct hammer strike upon the osteotome. The surgical team noted the same response as a brief but large patient spasm and requested TcMEPs to be tested. H-reflexes were significantly diminished for a period of approximately 5 min bilaterally. SSEPs remained undiminished while TcMEPs were diminished in amplitude but remained present in all recorded muscles bilaterally. Both H-reflexes and TcMEPs were determined to be unchanged from baselines at close and the patient awoke with no deficit

use of inhalants such as isoflurane and nitrous oxide [14]. Furthermore, H-reflex amplitudes show a concentration-dependent suppression in response to sevoflurane or propofol anesthesia [15, 16]. The same authors argue that both propofol and sevoflurane cause an increase of presynaptic Ia inhibition, a likely cause of H-reflex suppression [17, 18].

Previous authors have made suggestions regarding the limits of various anesthetic regimes whereby H-reflexes and F-responses are likely to remain valid [8]. The authors of this chapter can attest that H-reflexes and F-responses can be readily evoked by most anesthetic regimens that are appropriate for EMG, SSEP, and TcMEP monitoring, including total intravenous anesthetic, a mixture of volatile inhalants and propofol/remifentanil, or the use of up to 1.0 MAC of volatile inhalants. Although H-reflexes and F-responses are suppressed by these regimens to one degree or another, the stability of the H-reflex with stable anesthetic conditions has been established [11].

Stimulation Characteristics

Intraoperative H-reflexes are primarily evoked from *soleus* and *flexor carpi radialis* muscles in response to popliteal fossa and cubital fossa stimulation, respectively (Fig. 11.3). Stimulation

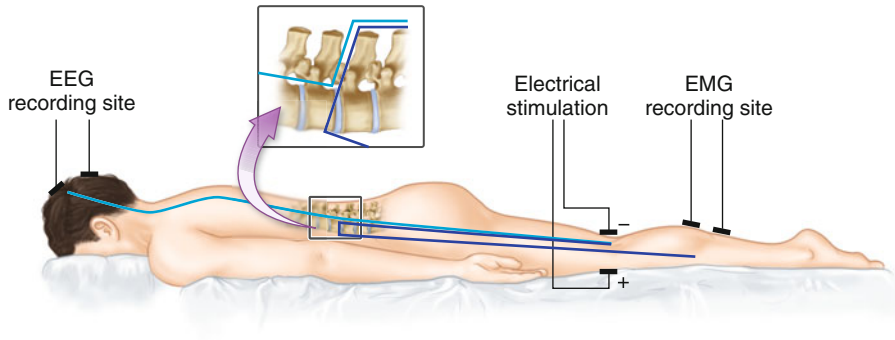

Fig. 11.3 Configuration of H-reflex testing. H-reflexes are most easily recorded from soleus muscle but can be recorded from multiple lower limb muscles in response to stimulation of the posterior tibial nerve at the popliteal fossa. Recording is typically bipolar at the soleus muscle. Stimulation can be bipolar at the popliteal fossa or monopolar across the joint as pictured above

can be achieved using needles or pads in a bipolar configuration or by placing the cathode in the popliteal/cubital crease with the anode placed on the opposite side of the joint [19]. The authors of this chapter have had considerable success with the latter, cross-joint stimulation configuration and prefer it, although it typically requires a higher stimulus intensity to evoke a H-reflex. The H-reflex is optimally activated by single pulses with relative long stimulus pulse widths of 0.5–1.0 ms. The stimulus pulse is typically monophasic and relatively low intensity. Although the first H-reflex response can often be elicited at a stimulus intensity below 10 mA, it is difficult to prescribe a specific stimulus intensity due to variables related to the individual patient and the selection of needle or pad electrodes for stimulation. Nevertheless, it can be said that the stimulus intensity to elicit a maximal H-reflex response should be near or even below the motor threshold. As stimulus intensity is increased, the H-reflex will reach maximal amplitude and then decline as the M-wave increases to its maximum (Fig. 11.4). Stimulus intensity should be chosen at the beginning of a procedure in order to maximize the H-reflex amplitude. Multiple H-reflex trials should be attempted in order to determine the stimulus intensity at which the H-reflex amplitude is maximized. Individual pulses should not be applied at intervals less than 1 pulse every 2.0 s (0.5 Hz stim rate). Some authors have even suggested that H-reflexes may be depressed by stimulating more often than once every 10 s [5, 20].

Recording Characteristics

In diagnostic or research settings, the soleus muscle is often selected for recording the lower limb H-reflex [7]. Commonly, one electrode is placed at the mid-calf, just distal to the bifurcation of the medial and lateral lobes of the *gastrocnemius* muscle. However, the medial gastrocnemius is also often targeted with bipolar needle electrodes over the medial aspect of the upper one-third of the calf [8]. We often use a referential EMG configuration with one needle over the *medial gastrocnemius* muscle and one over the *soleus* muscle. Recordings for the lower limb are single-sweep with a total sweep time of 50–100 ms. The medial gastrocnemius H-reflex response typically has a latency of ~30 ms, measured from the stimulus pulse onset, while the M-wave latency is closer to 15 ms or less. These numbers can vary with patient height or with conditions that affect peripheral conduction velocity. Since the M-wave, H-reflex, and F-response are recorded by EMG as CMAPs, the filter settings are similar to those used for free-running or triggered EMG. The high-pass and low-pass filters should be 3–30 Hz and 3–10 kHz, respectively. Notch filters to remove 60 Hz mains noise should generally be avoided.

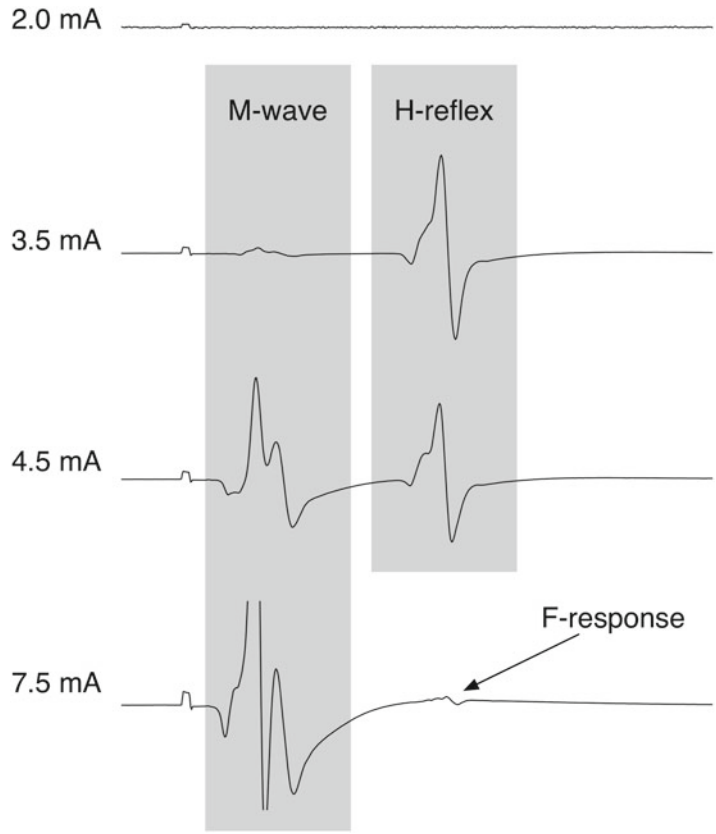

Fig. 11.4 Optimizing the H-reflex response. H-reflex amplitude will be affected by changing stimulus intensity. At low intensities the M-wave will be absent and a small H-reflex will appear. As stimulus intensity is gradually increased the H-reflex will peak in amplitude before declining as the M-wave comes to dominate the recording. F-responses can be noted at a similar latency to the now absent H-reflex

Recognizing the H-Reflex

When reviewing an EMG recording for potential H-reflex responses, the neurophysiologist should keep in mind the characteristics of the H-reflex. The H-reflex response should be of appropriate latency as discussed above, have a short duration, simple morphology, high amplitude relative to the M-wave, and should be characterized by stability across multiple trials. After consideration of the latency and amplitude of the recorded CMAP, the M-wave should be immediately distinguishable from the H-reflex. In contrast, the F-response may be confused with the H-reflex due to their similar latencies. However, the F-response differs in a number of key ways. Firstly, the amplitude of the F-response is typically considerably less than that of the H-reflex. Secondly the F-response is less stable than the H-reflex with respect to latency, amplitude, and morphology. Finally, the amplitude of the corresponding M-wave CMAP recorded along with the F-response is much larger than that which would typically be recorded with a H-reflex. This indicates supramaximal stimulation of the nerve, a condition that typically precludes the recording of H-reflexes. Other authors have noted that the H-reflex response at its peak will typically reach 50–100 % of the M-wave amplitude [21].

Assessing the H-Reflex

While sometimes used intraoperatively, there are no universally accepted criteria for interpreting H-reflex data. In addition, only a handful of primary papers have been published containing intraoperative H-reflex data [11–13, 22]. This makes the establishment of alarm criteria difficult. Factors that can be monitored for change

include peak-to-peak amplitude, latency of the response, and the ratio of the maximal H-reflex to maximal M-wave amplitude [23]. Although these elements can all be monitored, no objective criteria have been described relating to what would constitute an alarming alteration of these values. Nevertheless, the H-reflex has been described as remarkably stable given stable anesthetic conditions [11]. As such, the authors of this chapter recommend that H-reflexes be established at the beginning of a procedure and monitored for changes throughout the operation. Lacking any objective criteria, a decrease in amplitude of greater than 50 % and an increase in latency of greater than 10 % are reasonable and accepted criteria to use when deciding whether or not to communicate a change to the surgical staff. H-reflex changes correlating with changes of either SSEP or TcMEP are particularly alarming. Currently, the clinical utility of the F-response remains under investigation.

Troubleshooting the H-Reflex

As mentioned above, H-reflexes are recorded as an EMG response and are not recordable in the presence of neuromuscular blocking agents. Accordingly, a train-of-four test should be used to inform the neurophysiologist of the level of paralysis. If H-reflexes prove unobtainable at any point during the procedure, a train-of-four can eliminate neuromuscular blockade as a cause of signal loss.

It is not uncommon for the optimal stimulation intensity to vary during a surgical procedure. If the amplitude of the H-reflex or the maximal H-reflex to maximal M-wave ratio should decrease during the procedure, the first step should be to increase or decrease the stimulus intensity through multiple trials in order to optimize the H-reflex CMAP amplitude. The goal when testing H-reflexes should be to adjust the stimulus intensity to produce the maximal H-reflex response. The optimal stimulation intensity can drift by a few milliamps and may need to be retested. This could simply be due to a change in resistance of the stimulating electrodes.

Conclusions

The H-reflex is a useful tool for monitoring spinal cord excitability in the surgical suite. It can be run without disturbing the surgical staff, it does not require placing any electrodes beyond those commonly placed for more routine spinal cord monitoring modalities, and the response appears to be effected by anesthesia similarly to SSEP and TcMEP monitoring. Nevertheless, H-reflexes and F-responses are one of the least well-studied modalities applied intraoperatively. Unfortunately, only a handful of papers containing primary data exist. Moving forward, it will be necessary to further characterize these responses intraoperatively in order to continue to assess their value and to establish reliable alarm criteria for transmitting a warning to the surgical staff.

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Monitoring Procedures of the Spine

12

Denise Birkholz and Scott Francis Davis

The vertebral column is an extremely complex structure, and surgical procedures involving cervical, thoracic, and lumbar levels pose a risk to the neural elements. Although the overall incidence of a major neurologic complication such as paraplegia is low, advances in intraoperative neurophysiological monitoring (IONM) techniques have made multimodality monitoring an effective approach for preventing iatrogenic injury to the nervous system during spinal surgery.

Mixed nerve somatosensory evoked potentials (SSEPs) and transcranial motor evoked potentials (Tc-MEPs) are the IOM techniques most often used to monitor the spinal cord. Upper limb SSEP monitoring can also help prevent postoperative ulnar neuropathy and brachial plexopathy. However, these modalities are not sensitive to detecting spinal nerve root injury. Therefore, addition of electromyography (EMG) and triggered EMG can be used to monitor the spinal nerve roots.

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Spinal Anatomy

The spine is composed of 33 interlocking bones, surrounded by ligaments and muscles that provide the main support for the trunk and protect the spinal cord (Fig. 12.1). The 7 cervical, 12 thoracic, and 5 lumbar vertebrae are each separated by fibrocartilaginous discs that act as shock absorbers and allow the neck and back to move in multiple directions. Additionally, five fused vertebrae form the sacrum and four coccygeal bones form the tailbone or coccyx.

Each vertebra has critical functional parts. The vertebral body is the weight-bearing portion of the vertebra and is located anterior to the vertebral canal. Posterior to the vertebral body are bony projections that form the vertebral arch: bilateral pedicles, a lamina, transverse processes, facet joints, and a single posterior spinous process (Fig. 12.2). The vertebral canal contains the spinal cord or cauda equina, fat, ligaments, and blood vessels. Under each pedicle, spinal nerves exit the spinal cord and pass through the intervertebral foramen to branch out to the body. Surgeons often remove the lamina of the posterior vertebral arch to access and decompress the spinal cord or spinal nerves to treat spinal stenosis, tumors, or herniated discs.

The spinal cord extends from the foramen magnum to spinal level L1. At L1, the terminal portion of the spinal cord is called the conus medullaris. From the conus, a bundle of spinal nerves called the cauda equina further extend down to their respective vertebral level and exit.

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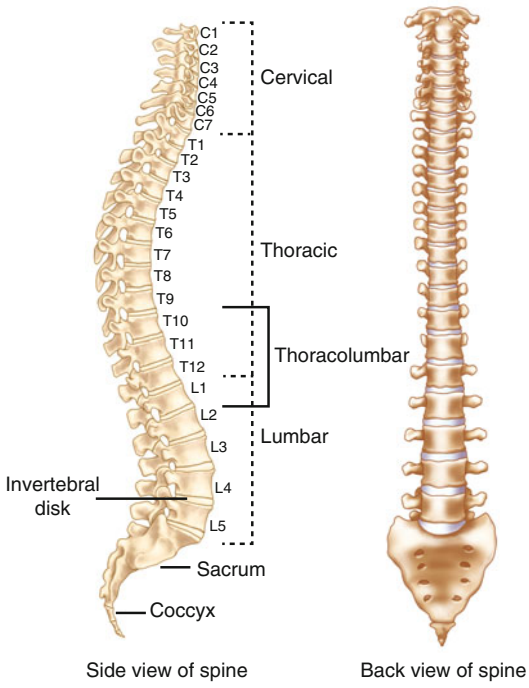

Fig. 12.1 (**a**) Lateral view and (**b**) posterior view of the spine. The cervical, thoracic, and lumbar vertebrae are separated by a cartilaginous disc that provides cushioning and allows for movement. The sacral and coccygeal vertebrae are already fused

Thirty-one pairs of spinal nerves emerge from the spinal cord (Fig. 12.3). There are 8 cervical spinal nerves, 12 thoracic nerves, 5 lumbar nerves, 5 sacral nerves, and 1 coccygeal nerve. Each spinal nerve is composed of motor and sensory fibers that pass through an intervertebral foramen between adjacent vertebrae. Cervical and thoracic spinal nerve roots exit laterally from the vertebral canal between adjacent pedicles, while lumbosacral roots extend downward as part of the cauda equina before exiting through foramina below the spinal cord. Nerve roots can be injured during surgery by electrocautery, drilling, retraction, or misplaced hardware.

Procedures of the Cervical Spine

The main function of the cervical spine is to support and move the head. The first cervical vertebra (C1) is often called the atlas and contains a bony ring, without a body, that connects directly to the skull. Together with the C2 vertebra, or axis, these two vertebral joints attach the skull to the spine and allow for movement of the head. Cervical spine surgery is generally performed to

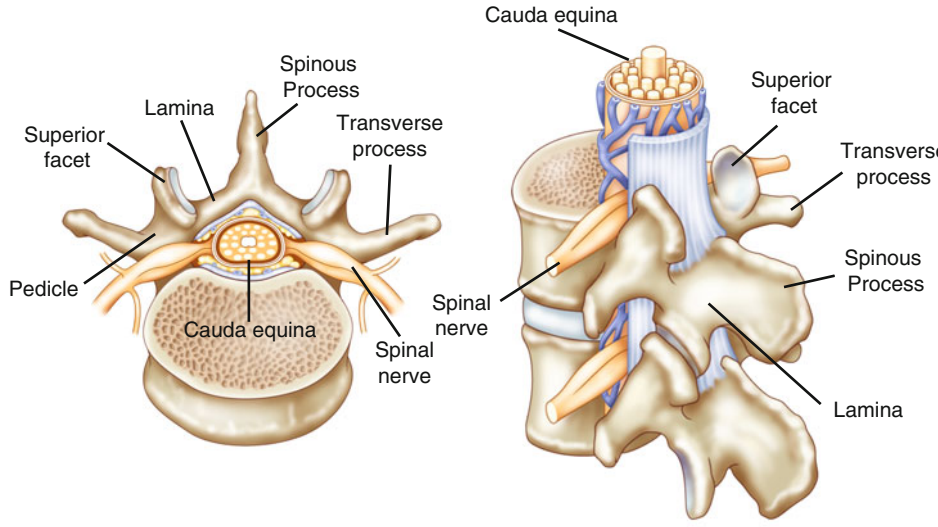

Fig. 12.2 Superior view of a vertebra showing the location of the critical functional parts relative to the spinal canal. The vertebral arch is formed from bilateral pedicles, lamina, transverse processes, facet joints, and a single posterior spinous process that protects the spinal cord and exiting nerve roots

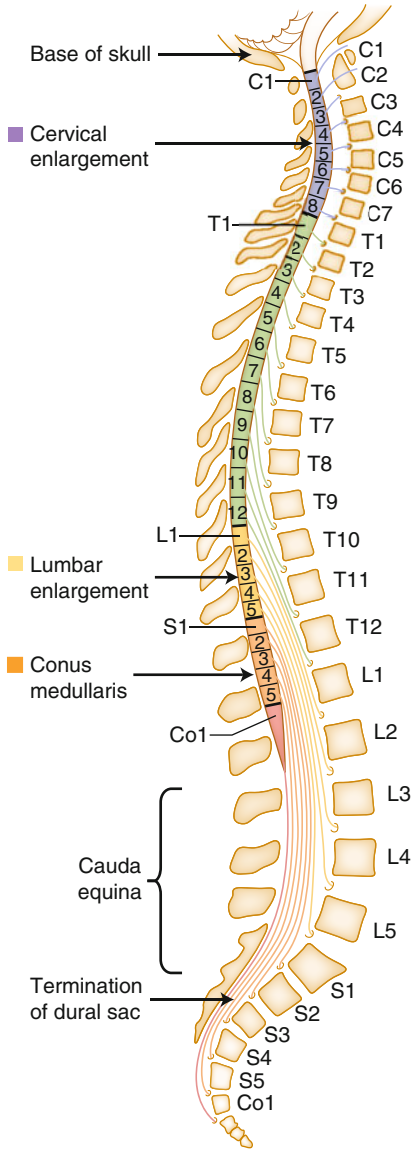

Fig. 12.3 Thirty-one pairs of spinal nerve roots branch off the spinal cord. Cervical and thoracic spinal nerve roots exit laterally from the spinal canal between adjacent pedicles, while lumbosacral roots extend downward as part of the cauda equina before exiting through foramina below the spinal cord

treat nerve impingements (radiculopathy), spinal cord compression (myelopathy), or spinal instability that is causing pain and weakness. Common cervical procedures include anterior cervical discectomy and fusion (ACDF), posterior cervical fusion (PCF), and cervical corpectomy. Risks during surgery include but are not limited to cord contusion, motor loss or weakness, peripheral nerve injury, or vascular compromise.

Injury to the C5 nerve root is the most common injury from cervical surgery and can result in pain, paresis, or paralysis of the shoulder. Other nerve roots are subject to postoperative palsy, but most complications occur at C5 due to its shorter length and more obtuse angle of exit from the foramen [1, 2]. The C5 nerve root is the only nerve supply to the deltoid muscle of the shoulder, so injury to the nerve root leads to an obvious weakness of this muscle and difficulty raising the arm to the side [2]. The potential for C5 palsies can been detected by using EMG and Tc-MEP monitoring during spinal surgery with specific focus on the deltoid and biceps brachii muscles. Brachial plexopathy resulting from positional or traction-induced injury may mimic C5 palsy [3]. Many surgeons maintain downward traction on the shoulders during a cervical surgery. Injury to the brachial plexus may result from this traction and can be detected by monitoring SSEPs during the procedure.

Anterior Cervical Discectomy and Fusion

ACDF is a procedure often performed to remove a herniated or degenerative disc. Narrowing of the vertebral canal, a condition called spinal stenosis, can cause chronic pain, numbness, and muscle weakness in both upper and lower extremities. Bone spurs can also develop resulting in foraminal stenosis thus compressing the exiting spinal nerves.

The surgical approach during an ACDF is from the anterior, or front, of the neck. An anterior approach allows the surgeon access to the disc space without disturbing the spinal cord, spinal nerves, and posterior neck musculature. An incision is made and midline structures and musculature are retracted to expose the vertebral bodies and disc space. Bone and disc fragments are removed in order to decompress the spinal cord and nerve roots. After the disc space is cleaned out, a bone graft is placed in a metal cage

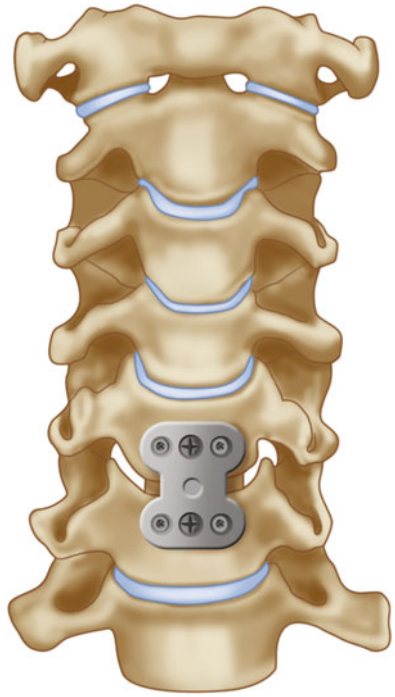

Fig. 12.4 Example of a metal plate and screws placed over the bone graft during ACDF surgery

and fit between the vertebral bodies. The adjacent vertebrae are held in place with a metal plate and screws. The ultimate goal of the surgery is to create a bony fusion between the adjacent vertebrae, which occurs as a result of the bone graft placement. The metal hardware simply acts as a cast, stabilizing the spine until fusion occurs (Fig. 12.4).

A common complication in anterior cervical surgery is vocal cord paralysis resulting from an injury to the recurrent laryngeal nerve (RLN). Patients with RLN palsy may experience hoarseness, develop a cough, or lose their voice completely and it may take several months for the nerve to recover [4, 5]. EMG monitoring using a special endotracheal tube has been shown to be useful in detecting injury to the RLN. Monitoring the RLN is discussed in detail in another chapter of this book.

Multimodality monitoring for anterior cervical fusions should include upper and lower SSEPs and Tc-MEPs to monitor spinal cord function, as well as EMG from the myotomes at risk to provide protection for the nerve roots. Positional injury may also be detected with upper extremity SSEP monitoring.

Posterior Cervical Fusion

If spinal stenosis cannot be relieved by an anterior approach, or if the patient's spine is not stable enough for this approach, the surgeon may opt for a posterior cervical laminectomy and fusion (PCF). The object of this procedure is decompression of the neural elements and stabilization of the cervical spine. Posterior fusions are also performed for instability of the cervical spine resulting from trauma or a degenerative pathology.

For PCF surgery, the patient is placed in a prone position (on their abdomen) with the head made immobile by placing in a special frame called a Mayfield (Fig. 12.5). The head is held in the Mayfield with pins. After the incision is made in the back of the neck, the surgeon will then dissect down through the subcutaneous tissues to the fascia overlying the spinous processes. Retractors are inserted to hold the muscle away from the spine, and the surgeon will begin to remove the lamina and other bony elements in order to decompress the spinal cord and nerve roots.

Various types of instrumentation are used to posteriorly fuse the cervical spine. Wiring can be used to stabilize the upper cervical vertebral segments (C1 and C2). Cervical vertebrae have anatomical structures not found elsewhere in the spine called the lateral masses, which are larger than the pedicles and are satisfactory targets for screw insertion. Placement of lateral mass screws and rods provides equal or greater biomechanical stability when compared to anterior plating or interspinous wiring techniques [6] (Fig. 12.6). Placement of lateral mass screws does not depend on the integrity of the laminae, pedicle, or spinous processes to achieve fixation as in case of cervical wiring and pedicle screws. The limitations of lateral mass fixation include risk of injury to the adjacent nerve roots, vertebral arteries, or facet joint [6, 7].

Similar to ACDFs, multimodality monitoring using SSEPs and Tc-MEPs to monitor the spinal cord and EMGs to monitor the nerve roots is the preferred monitoring plan for PCF.

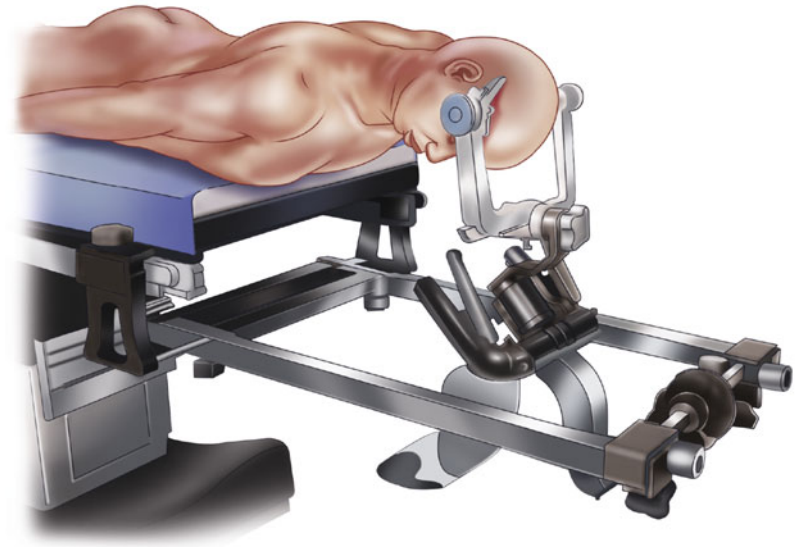

Fig. 12.5 Drawing of a patient positioned for a posterior cervical fusion using a Mayfield head frame

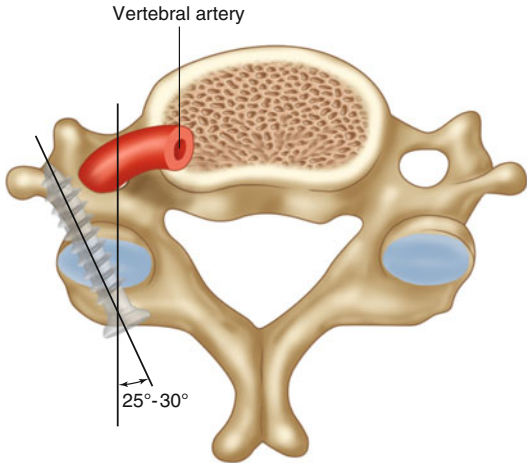

Fig. 12.6 Placement of lateral mass screws in a cervical vertebra

Cervical Corpectomy

When the cervical disease involves more than just the disc space or a single level, it may be necessary to remove the vertebral body and adjacent discs in a procedure called a corpectomy. This can be necessary for multilevel stenosis, tumor removal, or vertebral infection. The approach is similar to that of an ACDF. Once a majority of the affected vertebral bodies and disc material have been removed, a graft—typically shaped bone or a titanium cage—is fitted to support the anterior vertebral column (Fig. 12.7). The cervical spine is further stabilized with a metal plate and screws similar to that used in an ACDF. If the spine appears unstable after the anterior corpectomy, a PCF may be necessary to provide long-term stability. Recommended IOM is similar to that of an ACDF [8].

Procedures of the Thoracic Spine

The thoracic vertebrae—T1 through T12—provide attachment to the rib cage. Due to the presence of the ribs and position of the spinous processes, the thoracic spine is stiff and motion is limited. This immobility can put strain on the adjacent cervical or lumbar spine, making the areas from C6 to T2 and T11 to L2 especially susceptible to injury. Most commonly trauma or metastatic lesions are the cause of thoracic spine surgery. Thoracic laminectomy and fusion and corpectomy are performed similar to other levels. Burst fractures (discussed below) are often seen in the lower thoracic segments. Among the most

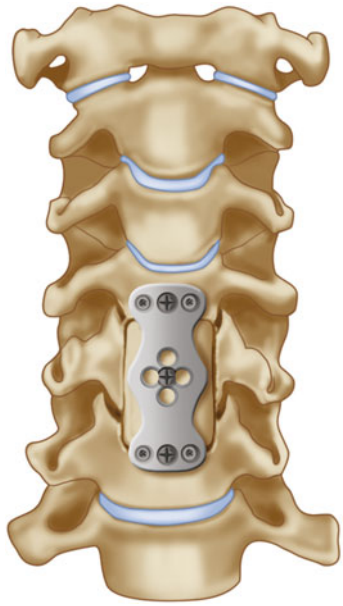

Fig. 12.7 Following removal of the vertebral body, a wedge-shaped bone graft is inserted into the space created by the corpectomy and is stabilized using a screw and plate system similar to an ACDF

commonly monitored procedures of the thoracic spine are for correction of scoliosis and spinal deformity.

Surgery for Scoliosis Correction

Scoliosis describes an abnormal, side to side, curvature of the spine. The two most common forms of scoliosis are degenerative and idiopathic (adolescent). Degenerative scoliosis is caused by a deterioration of the facet joints and occurs most commonly in people over 65. Surgery is often performed to reduce pain. Older patients may have osteoporosis and may require many levels of instrumentation to achieve a complete fusion. Idiopathic or adolescent scoliosis is seen in children and teenagers and usually is discovered during routine doctor's exams. It is necessary to prevent the curvature from progressing as the child ages. If the curve measures <20°, surgeons often choose to brace the spine or continue to observe the progression of the curvature. Surgery for adolescents with scoliosis is only recommended when the curvature is >45° and continuing to progress [9]. A high degree of curvature may put the patient at risk for cardiopulmonary compromise as the curve of the spine rotates the chest and decreases the vital capacity (ability to breathe).

Scoliosis correction procedures are extensive and may require both an anterior and posterior approach in severe cases. Correcting the scoliosis involves applying different forces to the spine including distraction and rotation. These maneuvers place the spinal cord at risk for either direct injury or regional ischemic injury as blood vessels become compressed.

Posterior fusion for scoliosis correction involves a long incision and exposure through the posterior musculature to access the bony elements of the spine. Instruments such as hooks and screws are attached to the vertebrae and serve as anchors for long rods that straighten and hold the spine in the correct position (Fig. 12.8). Bone graft is then added along the spine to facilitate a permanent fusion. An "anterior release" may be necessary prior to posterior instrumentation for patients with a severe deformity. This procedure is typically done with a lateral approach where the intervertebral discs are removed from the front to allow for more spinal movement and to encourage bony growth once the spinal curvature is corrected.

For corrections that are mainly needed at the thoracolumbar junction (T12–L1), the surgery can be performed via an anterior approach. The discs are removed to loosen up the spine, screws are placed in the vertebral bodies, and rods are used to reduce the curvature. An anterior technique has minimal blood loss and muscle damage compared to a posterior or anterior–posterior procedure. Additionally, not as many lumbar segments need to be fused thereby preserving some motion segments reducing the risk for future back pain. The anterior approach can only be done on thoracolumbar curves however and most idiopathic scoliotic curves involve the thoracic spine.

Multimodality spinal cord monitoring using SSEPs and MEPs has become a standard of care for scoliosis surgery. SSEPs may also help prevent postoperative neuropathy or plexopathy as these

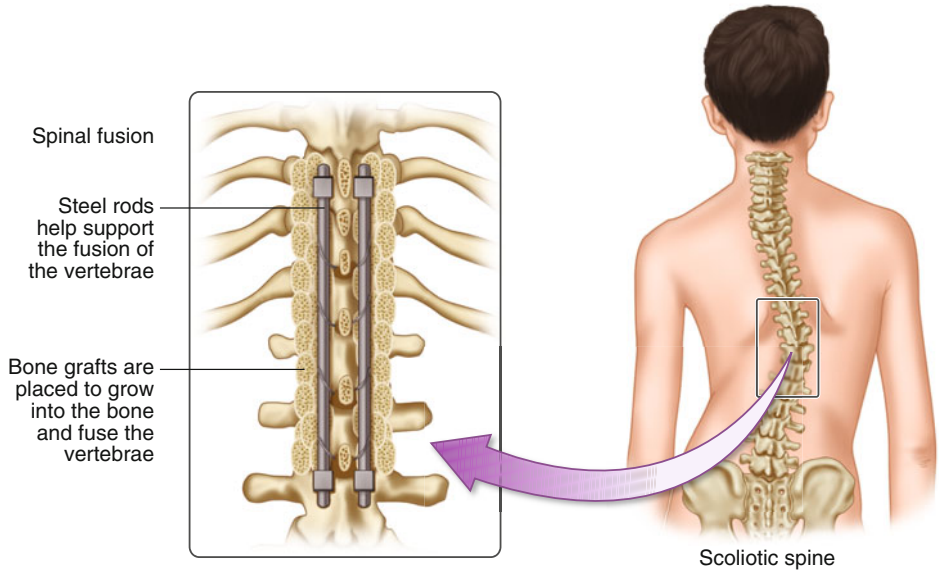

Fig. 12.8 On the *right* is an example of scoliosis. Notice the curvature creates an asymmetry that is visible in the stance of the patient. On the *left* is a corrected curve being held in place with rods. Bone graft is in place to facilitate bony fusion

procedures can be quite lengthy [3, 10, 11]. Injury to the thoracic spinal cord can produce abrupt bilateral or unilateral leg MEP loss and/or a decrease in lower extremity SSEP amplitude [12], and the surgeon can be immediately notified. While thoracic levels T2–T7 are not amenable to EMG monitoring, lower thoracic and lumbar levels can utilize free-running EMGs to reduce risk to spinal nerve roots. The anal sphincter should also be monitored when instrumenting at thoracolumbar levels due to the presence of the conus medullaris and risk to the extending cauda equina.

Thoracolumbar Trauma

Trauma to the spine indicates that an injury has occurred to any or all of the following components: bony elements, ligamentous (soft) tissues, and neurological structures. While injury does not always indicate the need for surgical intervention, mechanical instability and potential neurological injury are two concerns for spinal traumas. Instability is usually the result of a fracture in one of the major bony components (vertebral body, pedicles, lamina) of a vertebra. An unstable fracture may not allow the spine to withstand normal load-bearing activities without further risk of a neurologic injury. Classification methods for thoracolumbar fractures are based upon the mechanism of failure and the column of the spine affected. The spine is viewed as having three columns when viewed laterally. There is an anterior, middle, and posterior column [13] with the middle column the most important for stability (Fig. 12.9). Trauma to the spinal column can result in compression (burst) fractures, anterior and posterior element injuries with distraction, and anterior and posterior injuries with rotation [14]. Burst fractures can be highly unstable and generally occur when a violent compressive load results in failure of both the anterior and middle spinal columns. This severe compression of the vertebral body may be associated with extrusion of bony fragments into the vertebral canal putting at risk the spinal cord and cauda equina (Fig. 12.10). Burst fractures are treated by a procedure known as kyphoplasty. Guided by fluoroscopy, a needle is inserted into the vertebral body then a balloon is inflated to restore height, thereby creating a space where bone cement can be

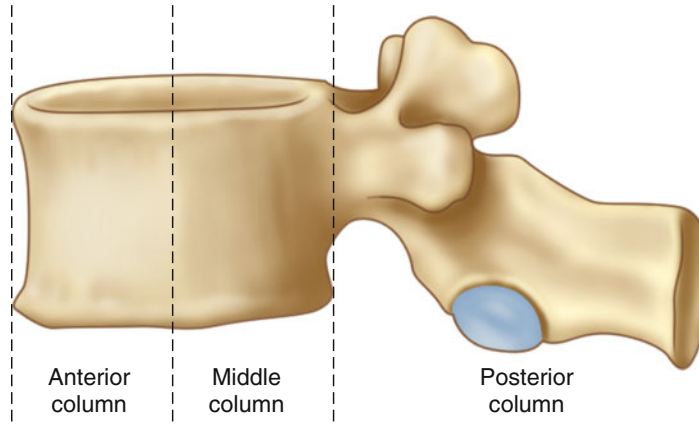

Fig. 12.9 The spine is viewed as having three columns when viewed laterally. The *middle column* is the most important for stability and load bearing

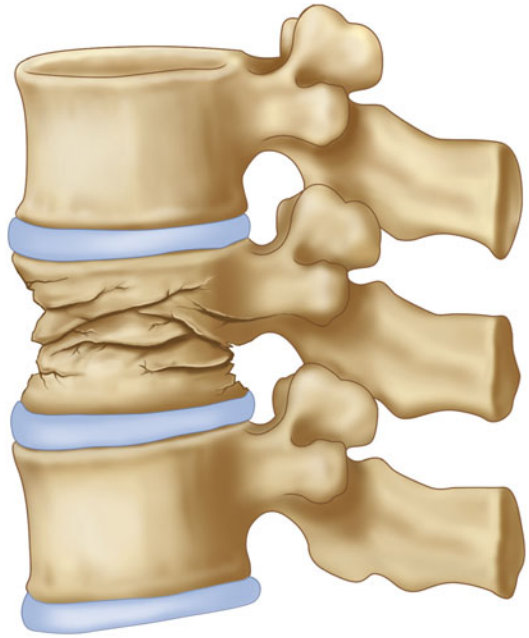

Fig. 12.10 An example of a burst fracture viewed laterally

injected to stabilize the fracture. Multimodality monitoring for trauma surgery of the spine can help reduce further injury to the neural elements as well as possibly providing information on the functional neurological status of the trauma patient that has just arrived to surgery from the ER.

Procedures of the Lumbosacral Spine

The lumbar spine—L1 through L5—supports the weight of the body. The vertebral bodies are much larger in order to absorb the stress of lifting and carrying. Below the lumbar region, the sacrum connects the spine to the hipbones. Below the sacrum, the coccyx completes the spine and provides attachment for ligaments and muscles of the pelvic floor. Common spine-related conditions that can cause lower back and lower extremity discomfort include disc herniation, degenerative disc disease, spondylolisthesis, spinal stenosis, and sacroiliac joint dysfunction. Minimally invasive (MIS) procedures such as a microdiscectomy or laminectomy may be able to relieve pain caused by central or foraminal stenosis. In the most serious cases, when the condition does not respond to conservative therapies such as physical therapy or pain management, a spinal fusion may be necessary to strengthen the spine and prevent motion in the vertebral segment(s) causing pain.

Below vertebral level L1, the vertebral canal contains the cauda equina. The cauda equina contains the lower lumbar and sacral spinal nerves traveling toward the appropriate level where they exit and innervate the lower extremity. Nerve roots can be injured during lumbosacral surgery

by retraction, compression, electrocautery, drilling, or misplaced hardware. One of the most common postoperative deficits is foot drop caused by injury to the L5 nerve roots. Other postoperative deficits can include numbness, weakness, and bowel or bladder dysfunction. SSEPs are not sensitive to detecting nerve root injuries; therefore free-running and triggered EMG along with Tc-MEP are the primary modalities most often used to monitor nerve root function. Depending on patient anatomy and the lumbar levels requiring fusion, there are different approaches to the spine that are utilized during surgery including posterior, anterior, and lateral approaches.

Posterior Lumbar Interbody Fusion

During a posterior lumbar interbody fusion (PLIF), the spine is accessed through an incision in the midline of the back and the large erector spinae muscles are retracted. Once the proper spinal levels are exposed, a laminectomy and often a discectomy are performed with the goal of decompressing the neural elements. If a discectomy is to be performed, it is followed by placement of a cage in the disc space (typically made of bone or synthetic material) that restores height to the disc space and assists in bone growth. Bone graft is added to provide a matrix for additional bone growth. The level is stabilized while fusion takes place using screws and rods (Fig. 12.11).

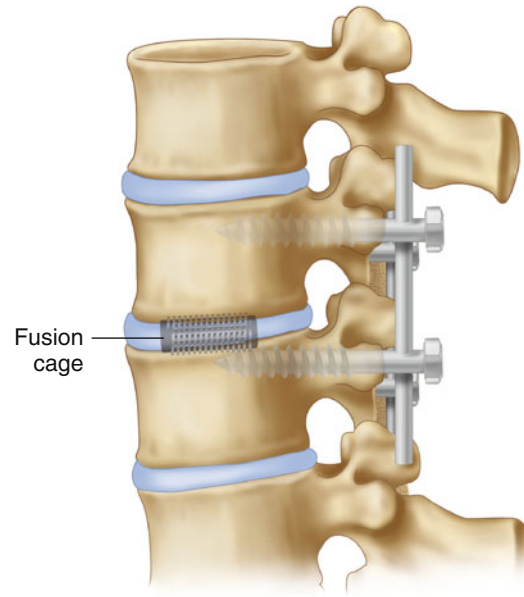

Fig. 12.11 The result of posterior lumbar interbody fusion. Following a laminectomy and discectomy, a bone graft was placed in the disc space. Screws and rods were inserted to stabilize the spine until the bony fusion is complete

The monitoring plan for a PLIF consists of upper and lower SSEPs to monitor the spinal cord and for positional injury [3, 10, 11]. Although the surgery is not at the level where spinal cord is present, the addition of SSEPs can still be useful in detecting ischemia as a result of hemodynamic changes.

Spontaneous EMG for nerve root monitoring is typically recorded continuously during surgery, so it is very important for anesthesia to not administer any neuromuscular blockade after intubation. Activity is recorded from myotomes corresponding to the nerve roots at risk, and irritation resulting in "train firing" or "neurotonic discharge" should be immediately reported to the surgeon. In addition to free-running EMG, stimulus-triggered EMG has become a standard technique used during pedicle screw insertion. Triggered EMG relies on the concept that intact cortical bone should electrically insulate a properly placed pedicle screw from the adjacent nerve root. By stimulating the pedicle screw directly using a monopolar probe, a properly placed screw should not elicit any muscle response below a stimulus of 10 mA. With a medial pedicle breach, either directly by the screw or from a crack in the pedicle wall, electrical stimulation will activate adjacent nerve roots, evoking compound muscle action potential (CMAP) responses in muscles from the appropriate myotomes at a stimulus <7 mA [15–17]. Some types of pedicle screws, such as those coated with hydroxyapatite, have an extremely high electrical resistance and cannot accurately or safely be stimulated [18]. In these cases, stimulating the pilot or tapped hole prior to placement of these screws is recommended. Patients with advanced osteoporosis may have lower than

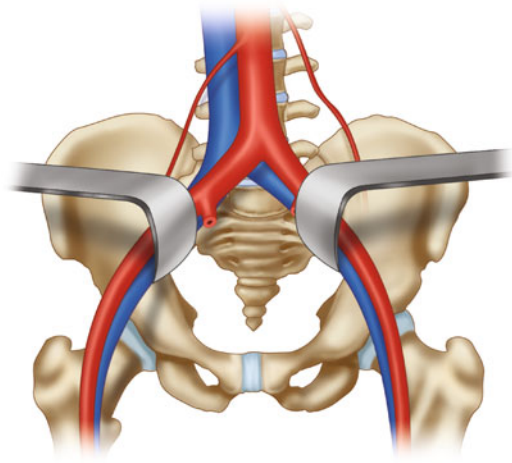

Fig. 12.12 Retraction of major blood vessels is required for access to the vertebral bodies and disc space during an ALIF

expected impedances and may trigger false-positive responses. Alternatively, patients with chronically compressed nerve roots may require a much higher stimulus intensity to evoke a CMAP response. The surgeon may also wish to stimulate a nerve root directly using T-EMG for identification or to test function.

Anterior Lumbar Interbody Fusion

An alternative to the PLIF is an anterior lumbar interbody fusion (ALIF). For this procedure, the spine is accessed through an abdominal incision usually on the left side. A common retroperitoneal approach allows access to the spine without disturbing abdominal structures. The anterior approach gives better access to the disc space so more disc material to be removed and a larger spinal implant to be used. With an ALIF, there is minimal damage to the large stabilizing spinal muscles and the spinal nerves remain largely undisturbed. The procedure is performed in close proximity to the major blood vessels (aorta, iliac artery, vena cava, and iliac vein) that supply the legs [19, 20]. Vascular surgeons often assist in retracting the blood vessels during exposure for these procedures (Fig. 12.12). Lower extremity SSEPs are performed while retractors are in place to monitor for vascular compromise.

Minimally Invasive and Lateral Approaches to the Lumbar Spine

MIS approaches to spine surgery are designed to offer decompression and fusion through a smaller incision resulting in reduced tissue damage, blood loss, less postoperative discomfort, and a quicker recovery time. Procedures such as a microdiscectomy or laminectomy can be done through a very small incision and the insertion of tubular dilators to enlarge the space (Fig. 12.13). The procedure is accomplished through a tube or small tunnel. IOM can be valuable to the surgeon during these procedures because the incision is small and the spine is not largely exposed, making anatomical landmarks challenging to identify [21].

A lateral approach to perform a spinal fusion is considered a MIS spine surgery [22]. Instead of a long posterior or anterior incision, the surgeon makes one or more smaller incisions on the patient's side and uses a dilator/retractor system to expose and visualize the spine. A lateral approach does not require major organs or blood vessels to be moved. Once the spine is exposed, a standard discectomy is performed and a large cage is implanted in the disc space. A lateral plate or posterior instrumentation may be used to further secure the implant and stabilize the spine.

To access the disc space, the surgeon must navigate through the large psoas muscle and in close proximity to nerves of the lumbosacral plexus (Fig. 12.14). Free-running and triggered EMGs are critical during lateral approaches as these modalities can help identify the location of nerves in the lumbar plexus during exposure and retractor placement. Upon placement of the retractor, the surgeon may wish to further verify the absence of neural tissue with an electrically stimulated monopolar probe. While not as routinely used as EMGs during lateral procedures, lower extremity SSEPs can be utilized to monitor the nerves of the lumbar plexus, and both upper and lower extremity SSEPs can be used to monitor positional effects.

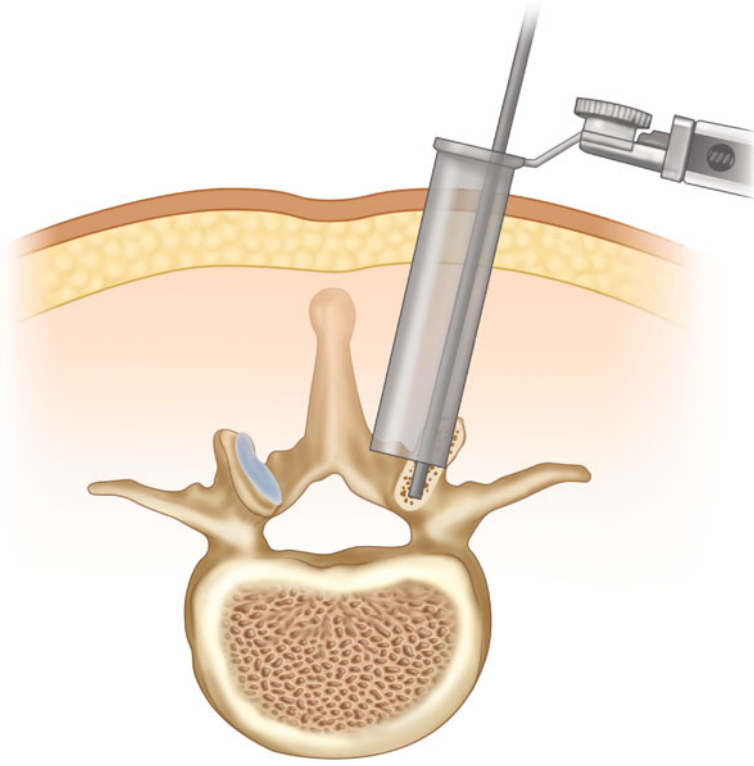

Fig. 12.13 Minimally invasive approaches to spinal surgery involve the use of tubular dilators for access

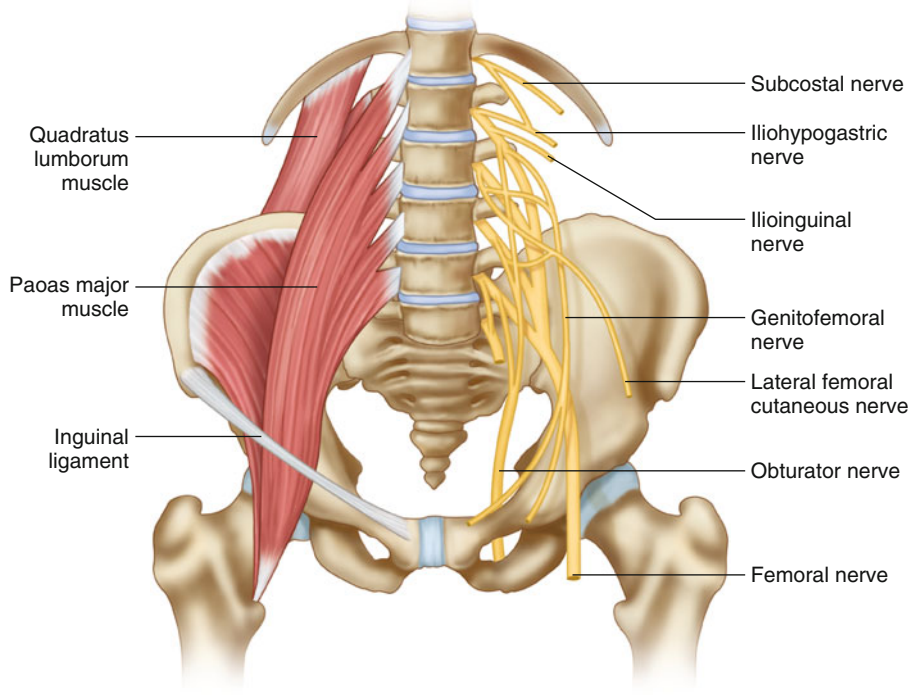

Fig. 12.14 The transpsoas approach to lateral access spine surgery puts elements of the lumbar plexus at risk

Conclusion

Spine surgery places at risk the spinal cord, nerve roots, nerve plexuses, and peripheral nerves. A multimodality approach to intraoperative monitoring utilizing SSEPs, Tc-MEPs, and EMGs can provide real-time feedback to the surgical team and reduce the risk of permanent neurologic injury.

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Intraoperative Monitoring for Surgery of the Spinal Cord and Cauda Equina

13

Scott Francis Davis and Jim Higgins

Introduction

The spinal cord is the conduit by which sensory input and motor output influence human behavior. Although the function of the spinal cord mostly involves moving information to and from the brain, there are several important functions that are regulated at the level of the cord and even more functions that local spinal cord circuits influence or modulate. Surgery of the spinal cord or cauda equina carries with it the risk of serious complications, including paralysis and other morbidities that have the potential to negatively impact the quality of life of a patient forever [1, 2]. Nevertheless, there are certain pathologies that have no other treatment option than surgical intervention [3–5]. Intraoperative monitoring and mapping of the spinal cord and cauda equina are helpful for protecting spinal cord function during surgery as well as providing the surgeon with real-time functional information that may allow more aggressive and complete treatment of the pathology [6–8]. This chapter will discuss spinal cord monitoring for surgery to remove intramedullary spinal cord tumors and for spinal cord untethering.

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Iatrogenic Injury to the Spinal Cord

The spinal cord can become injured during surgery to remove lesions or correct anomalies. Often a neurologically intact patient will be diagnosed with a spinal cord tumor that is life threatening and must be removed. The tumor may have been slow growing enough that the patient never developed any neurological symptoms, but on imaging it is difficult to see any remaining spinal cord at the level of the tumor. The surgeon is faced with the difficult task of removing the lesion without causing a new permanent postoperative injury. It may be unlikely that the patient in this example will wake up from surgery with the tumor completely removed and have no neurological deficits, but if there is any chance, it will be because the surgeon made use of intraoperative monitoring and mapping during the procedure.

The mechanisms of iatrogenic injury that can potentially be prevented through spinal cord monitoring are distraction, compression, and vascular compromise during the exposure and resection of the lesion. Retraction as well as surgical maneuvers near the spinal cord may cause local spinal cord ischemia that can be potentiated by the use of controlled systemic hypotension as a means of hemostasis. Routine multimodality spinal cord monitoring using somatosensory evoked

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potentials (SEPs) and transcranial motor evoked potentials (MEPs) are the best indicators of impending spinal cord injury. There may be visual cues of hemodynamic causes of impending spinal cord injury, such as blanching of the cord, but this should never be the preferred method of monitoring. If local ischemia is suspected, immediate increase of the systemic blood pressure is often effective at reversing the change in monitoring data and protecting the spinal cord from permanent ischemic damage. Retractor placement should also always be suspected when monitoring changes are observed.

Intramedullary Spinal Cord Tumors

Intramedullary spinal cord tumors are growths that occur within the substance of the cord and arise from cells of the spinal cord. The most common types of intramedullary tumors are astrocytomas, hemangioblastomas, and ependymomas [9]. This tumor type is rare and accounts for approximately 2–4 % of all spinal cord tumors. Usually slow growing and benign, patients often experience no neurological symptoms initially, instead complaining only of back pain. Neurological complications arise later in the course of the disease as the tumor begins to displace more and more normal spinal cord tissue. Complete resection of intramedullary tumors is the only curative treatment, and results are best when surgery is performed earlier in the disease process while the tumor is still small.

Surgical Procedure

Patient Positioning

Surgery to remove intramedullary spinal cord tumors is done with the patient prone on a Wilson frame or on jelly rolls. A Mayfield device is used to immobilize the head for cervical and high thoracic procedures, but not for lower thoracic lesions. As with many types of surgery, the use of SEPs can help detect peripheral nerve/plexus injury secondary to positioning.

Anesthesia

Intraoperative monitoring of SEPs, MEPs, and D-waves will be an important consideration for the anesthesiologist when deciding upon an anesthetic regimen for the procedure. A total intravenous anesthesia (TIVA) regimen using propofol or dexmedetomidine combined with a narcotic is the preferred regimen to insure high specificity of intraoperative monitoring modalities [10, 11].

If it is necessary to employ halogenated agents, they should be minimally used, generally at doses at <1/3 MAC. It is also undesirable to change agents during the procedure as the doses are additive.

The avoidance of muscle relaxants is necessary for MEP monitoring, although occasionally this will produce some trepidation on the part of the surgeon or anesthesiologist as the surgeon will be working within the spinal cord and cannot tolerate any patient movement. Partial neuromuscular blockade has been used with some success, but careful titration is necessary in order to prevent a compromise of the IOM data [12].

Contraindications for MEPs should be documented and include a pacemaker, history of seizure, or metal implants in the head. The relatively low risk of running MEPs, even with a patient history of seizure, should be weighed carefully against the benefit of having real-time information about spinal cord function available during surgery. The anesthesiologist should place a bilateral soft bite block between the molars to prevent tongue and lip laceration during MEP stimulation [13].

Approach

The most common approach to access the tumor is through a dorsal myelotomy. Under microscopic guidance, the arachnoid is opened and secured to the dural edges. A cut is sharply made down the posterior median sulcus dividing the dorsal columns. Occasionally, midline must be approximated due to distortion of the tissue because of the tumor. Tumors that lay more lateral than medial may sometimes be accessed through the dorsal root entry zone instead of a midline myelotomy.

Resection

In the best case scenario, there is a clear plane between the tumor and the spinal cord. The tumor is dissected from the parenchyma of cord sometimes using an ultrasonic aspirator. The last part of the tumor to be liberated is the ventral portion, which receives its blood supply from the anterior spinal artery. Following resection, the meningeal layers are closed, as are the subcutaneous tissue layers and the skin [14].

Monitoring for Intramedullary Tumors

The goal of intraoperative monitoring for resection of intramedullary spinal cord tumors is to maximize tumor resection while preserving neurologic function to the greatest extent possible. Multimodality spinal cord monitoring includes the use of SEPs and MEPs. Upper extremity SEPs are most useful when monitoring for the removal of cervical lesions or to monitor for positional related neuropathy during procedures of the thoracolumbar cord. Lower extremity SEPs are useful for removal of thoracic lesions.

MEPs monitor the functional integrity of the motor pathways and are highly specific for the corticospinal tract and the vascular territory of the anterior spinal artery. SEPs should never be run exclusive of MEPs for intramedullary tumor removal. Surgery for removal of intramedullary spinal cord tumors, due to the microsurgical technique involved, carries with it a more likely risk of discrete (sensory or motor) injury than other types of surgery [14].

SEPs are most critically monitored during midline myelotomy and should be run continuously during this early phase of surgery. SEPs may be lost, however, following myelotomy [15]. MEPs become important during work at the cleavage plane between the tumor and spinal cord. Unlike SEPs, which may be continuously run, MEPs cause patient movement and require a pause in surgery before stimulation [16].

Traditional MEP monitoring uses a train of transcranial square wave pulses to activate the primary motor cortex and corticospinal tract as it descends in the internal capsule [16]. Each pulse delivered during MEP monitoring results in direct activation of the corticospinal tract as well as indirect activation of the pathway through synaptic interactions in the primary motor cortex (see Chap. 7 on motor evoked potentials). The action potentials resulting from direct activation of the white matter tracts are known as D-waves (for Direct activation) [17]. The D-waves summate at the alpha motor neurons bringing them to threshold resulting in lower motor neuron firing and contraction of distal musculature. It is the resulting muscle contractions which cause patient movement and make MEPs impractical for continuous monitoring during resection.

By placing epidural spinal electrodes, it is possible to record the D-wave resulting from a single transcranial pulse as it travels along the corticospinal tract in the spinal cord [18]. This single transcranial pulse while enough to elicit a D-wave is insufficient to cause depolarization and firing of the lower motor neurons. This makes D-wave monitoring ideal for continuous monitoring of corticospinal tract function during resection of intramedullary spinal cord tumors (Fig. 13.1). D-wave monitoring is also 100 % specific for the corticospinal tract unlike muscle MEPs that depend on the function of additional descending pathways [19].

Sala and colleagues have shown that D-waves are the strongest predictor of motor outcome [19]. Warning criteria for D-wave monitoring are well established with a 50 % amplitude reduction being significant for permanent motor deficit [20]. D-wave amplitude reductions tend to be gradual allowing time for intervention if the neurophysiologist begins to notice a trending amplitude reduction. Sometimes a simple pause in surgery or change in approach will reverse a mild amplitude decrease. Warm irrigation and hypertension are also often successful treatments. Reduction in D-wave amplitude that does not reach 50 % may be a harbinger for temporary motor deficit postoperatively, but this carries an excellent prognosis for recovery [20]. Latency shifts in the D-wave signal have not been found to be clinically significant.

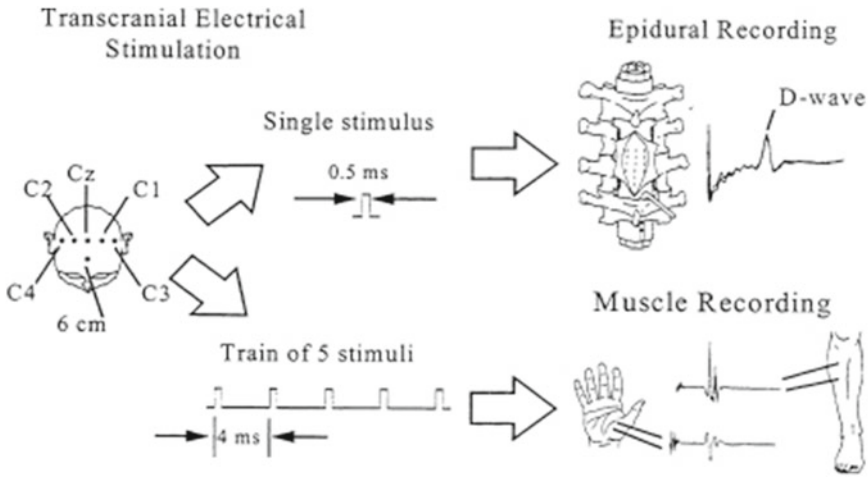

Fig. 13.1 Transcranial stimulation over the motor cortex using a single square wave pulse results in a recordable D-wave from an epidural electrode. Pulse train stimulation will produce a volley of D-waves sufficient to depolarize lower motor neurons and subsequent recording of compound muscle action potentials from the distal musculature

For complete monitoring of motor function, D-waves should be run continuously during resection with occasional pause in surgery to run a muscle MEP [21, 22]. The criteria for interpretation of the muscle MEP remain presence or absence of the CMAP response and should be interpreted in conjunction with D-wave data. Generally, loss of muscle MEP recordings predicts a subsequent loss of D-wave amplitude if no correction is taken. Loss of the muscle MEP with preservation of D-wave amplitudes will not serve as an indication to abandon the surgery; however this situation will result in a temporary postoperative motor deficit with subsequent recovery [19] (Fig. 13.2). Loss of muscle MEPs with preservation of D-waves is thought to occur due to injury to other descending motor pathways with preservation of the corticospinal tract. The D-wave is generated exclusively by the corticospinal tract, while other descending pathways contribute to the muscle MEP [19]. Injury to these additional motor pathways may be compensated for by the intact corticospinal tract accounting for recovery of motor function in the days, weeks, or months following surgery.

Tethered Spinal Cord

Tethered cord is the name of a constellation of symptoms that occur as a result of abnormal attachment of the spinal cord to other tissues that limits its movement within the thecal sac [23]. There are several causes of tethered cord with the most predominant cause being spinal dysraphism (a type of neural tube defect) [23]. Spinal dysraphisms may be open or closed (occult) (Fig. 13.3). Open dysraphisms include myelomeningocele where the spinal cord and meninges protrude from the child's back and meningocele where just the meninges are protruding from the back and the spinal cord remains in place. There is occasional association of a benign fatty tumor, a lipoma that attaches to the spinal cord and is covered by skin. This is called lipomyelomeningocele and is a type of occult spinal dysraphism. The various attachments of the spinal cord exhibited in these conditions prevent the spinal cord from ascending to the T12–L1 vertebral level during postnatal growth. This causes metabolic changes in the caudal spinal cord (the conus

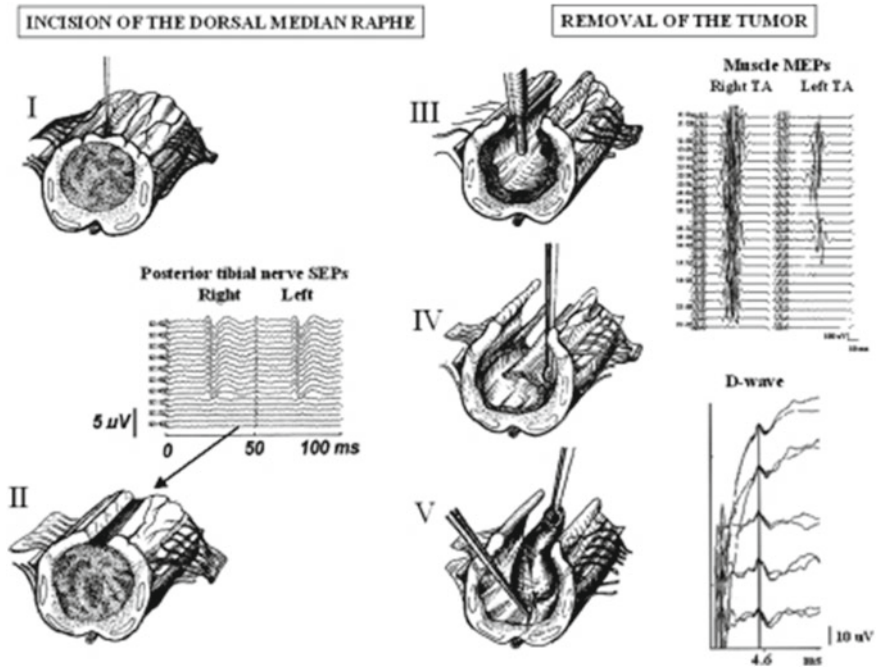

Fig. 13.2 Lower SEP, MEP, and D-wave recordings during removal of an intramedullary tumor. The stages of tumor removal are shown I–V. Lower SEP recordings were lost following midline myelotomy (II) followed by subsequent loss of left lower extremity MEP recordings. D-wave amplitude, however, remained unchanged allowing the surgeon to continue the resection. In a case such as this, a temporary paralysis of surgery can be expected with excellent prognosis for return of motor function

medullaris) as a result of spinal cord stretch and vascular insufficiency [24]. The cauda equina is also stretched including the sacral nerve roots that mediate bowel and bladder function. See Chap. 2 for anatomical review of the spinal cord and cauda equina.

Symptoms of tethered spinal cord include back pain, leg pain and weakness, and bowel and bladder incontinence among others [25]. Visual signs in children include a hairy patch over the sacral region, a skin growth, or a depression known as a sacral dimple. If mild, tethered cord may go undiagnosed until adulthood [25]. Diagnosis is made on imaging studies (MRI, CT, myelogram, or ultrasound) [26]. Surgical untethering is the only effective treatment for this condition.

Surgical Procedure

Patient Positioning and Approach

The patient is placed in the prone position, and a skin incision is made over the vertebral segments containing the defect. A laminectomy is performed exposing the dura. The dura is then incised in order to access the lesion involving the conus medullaris and cauda equina.

Anesthesia

The recommended anesthesia regimen is similar to what is recommended above for the removal of

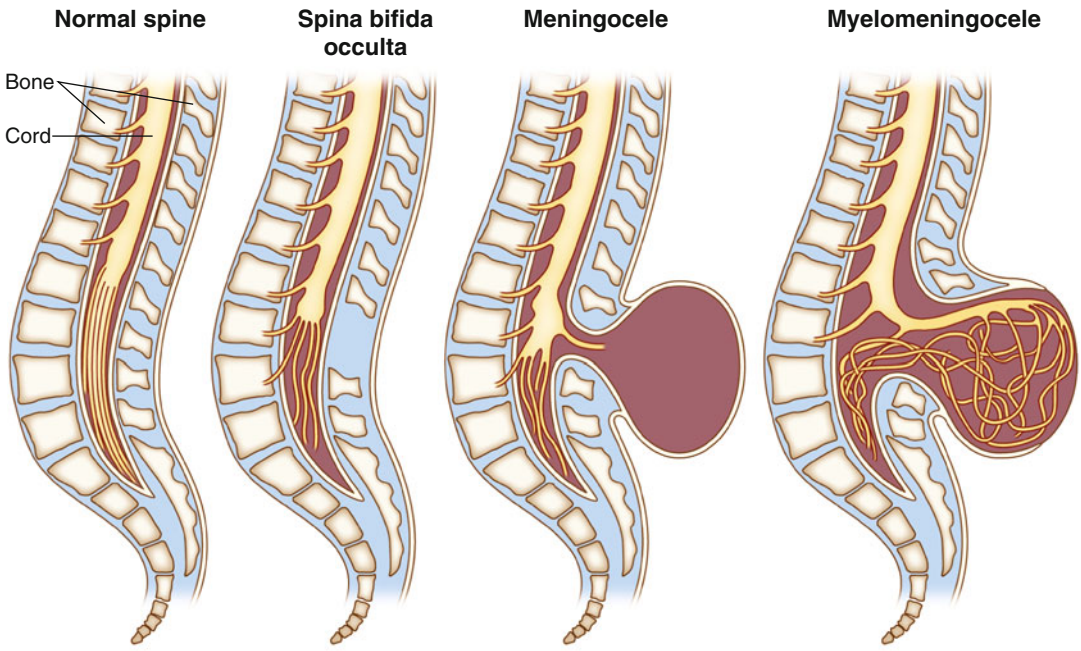

Fig. 13.3 Illustration showing the characteristics of spina bifida occulta, meningocele, and myelomeningocele

intramedullary spinal cord tumors. The avoidance of neuromuscular blockade is of utmost importance for tethered cord surgery due to the importance of both EMG and MEPs for this procedure. 4/4 twitches should be considered essential for effective monitoring.

Untethering

Once the neural elements are reached, the nerve roots are identified and freed from their attachments. The filum terminale is also identified, and if it is contributing to the tethering of the cord is cut. This stage of the procedure poses the most risk to the neural elements. After the cord has been untethered, it is free to ascend in the spinal canal. Injury to the spinal cord can happen at this time if there is any "spring back" of the cord as the filum is cut [26].

Monitoring for Tethered Cord

A multimodality approach is used for monitoring of tethered cord surgery [8, 27, 28]. SEPs, while not generally protective of individual nerve roots, may be used to offer more complete and continuous spinal cord protection than MEPs alone. The proximity of surgery to the conus and the potential for contusion as the cord is released are indictions for SEP monitoring.

The greatest risk during the procedure is to the nerve roots of the cauda equina. Spontaneous EMG is used to monitor the activity of the nerve roots during the procedure [27]. Similar to the use of EMG for other surgeries of the spine, single CMAP responses or small bursts are not clinically significant and may be used by the surgeon to guide the dissection. The use of an audio monitor for EMG is highly suggested for this purpose.

Triggered EMG is used to help the surgeon identify functional nerve roots [28, 29]. Often the surgeon is unable to visually identify nerve roots in the presence of tissue adhesions or a lipoma and will rely on electrical stimulation to discriminate between neural and nonneural tissue [30]. Furthermore, stimulation of the nerve roots can help identify their level of origin and whether or not they are healthy [29]. A healthy nerve root will have a stimulation threshold under 2.0 mA,

whereas a pathologic nerve root will have a higher threshold to stimulation. It is important when stimulating that the surgical field be dry and good contact is made between the electrode and the tissue to avoid any current shunting. A bipolar handheld probe is typically used to maximize specificity when stimulating. Electrical stimulation for the purpose of identifying nerve roots or identifying nonneural tissue to excise is often a time of high anxiety for the neurophysiologist as the absence of a response is taken as an indicator that the tissue in question can be cut. This is often the case when the surgeon is seeking to identify and cut the filum terminale to untether the cord [28–30]. For this reason, it is of utmost importance that the surgeon be encouraged to first find and test a functional nerve root so that the adequacy of stimulation and recording can be verified.

Verifying the identity of the nerve roots is only possible if a sufficient number of recording channels are available for the inclusion of multiple muscles [30]. Furthermore, the recording montage must be bipolar (muscles cannot be referenced together) in order to have adequate specificity.

EMG monitoring of the anal sphincter is necessary due to the risk of injury to both the conus and the S4 nerve root [31]. Bilateral recording from the external anal sphincter involves the placement of four needle electrodes in the sphincter muscle. It is important to make sure the electrodes are placed in the muscle itself and not in the skin lateral to the muscle.

The use of MEP monitoring for tethered cord surgery is important [32]. MEPs provide protection of the motor tracts and the vascular territory of the anterior spinal artery. MEP monitoring is very sensitive to ischemia, which is a significant risk during this procedure. Muscles monitored for MEPs should include not only the intrinsic foot muscles (as would be recorded for any surgery where MEPs are monitored) but all of the muscles that are being monitored by EMG as well. When a TIVA regimen is used, MEP monitoring may be highly specific for nerve root injury and is a useful adjunct to EMG monitoring. Alarm criterion for spinal cord injury is loss of the most distal muscle response. A loss of response from a more proximal muscle may be an indicator of injury to the nerve roots innervating that muscle. MEP recordings should be obtained as often as practical during surgery including the time from untethering through closing. This is necessary in order to monitor for emerging spinal cord injury resulting from the untethering.

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Monitoring Posterior Fossa Craniotomies

14

Denise Birkholz and Scott Francis Davis

The base of the skull is divided into three cranial fossae: posterior, middle, and anterior (Fig. 14.1). The posterior fossa is the deepest and largest and is enclosed by the occipital bone. Within the posterior fossa are the brainstem and cerebellum. The brainstem—consisting of the midbrain (mesencephalon), pons, and medulla—contains the nuclei of cranial nerves (CN) III–XII and is responsible for vital autonomic nervous system function. The brainstem also contains afferent and efferent fiber tracts that connect the brain with the rest of the body. The cerebellum is responsible for movement, balance, and coordination. Due to the complex anatomy and close proximity of these vital structures to each other, the use of intraoperative neuromonitoring (IOM) during posterior skull base surgery can aid the surgeon in identifying neural structures at risk as well as verifying neural integrity once the decompression is complete. This chapter focuses on surgeries for microvascular decompression (MVD), vestibular schwannoma, and Chiari malformation and the modalities used to preserve the neurological function of cranial nerves and brainstem structures during these types of surgeries.

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Microvascular Decompression

MVD is a procedure to relieve symptoms caused by vascular compression of a nerve. When medication does not provide relief, an MVD surgery is an option to treat syndromes such as trigeminal neuralgia, hemifacial spasm, and the less common glossopharyngeal neuralgia (not discussed in this section). To gain access to the offending vessel and the affected nerve, an incision is made behind the ear on the side of the head where the patient feels pain. A portion of the skull is removed and the dura is opened to expose the cerebellum. The cerebellum is moved out of the way, exposing the brainstem. Typically under a microscope, the arachnoid layer is dissected away allowing for visualization of the facial nerve (CNVII), the vestibulocochlear nerve (CNVIII), and finally the trigeminal nerve (CNV). The surgeon places a tiny sponge between the compressing vessel and the nerve, isolating the nerve from the pulsating effect and pressure of the blood vessel (Fig. 14.2).

During surgery to address cranial neuralgias, surgeons typically opt to monitor the trigeminal nerve (CNV) and the facial nerve (CNVII), using free-running EMG and triggered EMG. The trigeminal nerve is monitored by placing needle electrodes in the masseter or temporalis muscle.

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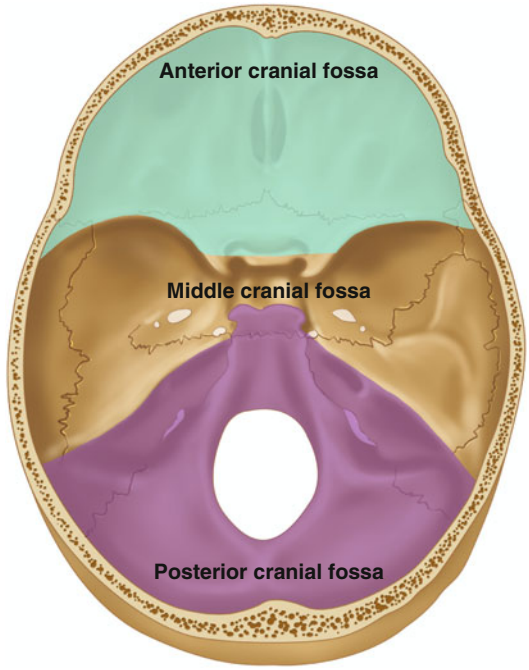

Fig. 14.1 Anterior, middle, and posterior cranial fossae

Facial nerve monitoring is accomplished by placing electrodes in muscles of the five main branches of CNVII that control facial expression: temporal, zygomatic, buccal, marginal mandibular, and cervical. EMG monitoring is helpful in locating cranial nerves and determining adequate decompression. A complication of MVD surgery is ipsilateral hearing loss from injury to the vestibulocochlear nerve. Brainstem auditory evoked potentials (BAEPs) are used to help prevent injury to CNVIII due to traction, ischemia, or cautery. BAEPS are also utilized when there is risk of brainstem ischemia associated with manipulation of the cerebellum.

Trigeminal neuralgia, also known as tic douloureux, is an inflammation of the trigeminal nerve causing extreme pain and muscle spasms in the face. Attacks of intense, electric shock-like facial pain can occur without warning or be triggered by touching specific areas of the face. The trigeminal nerve functions in sensing facial touch, pain, and temperature, as well as controlling muscles used

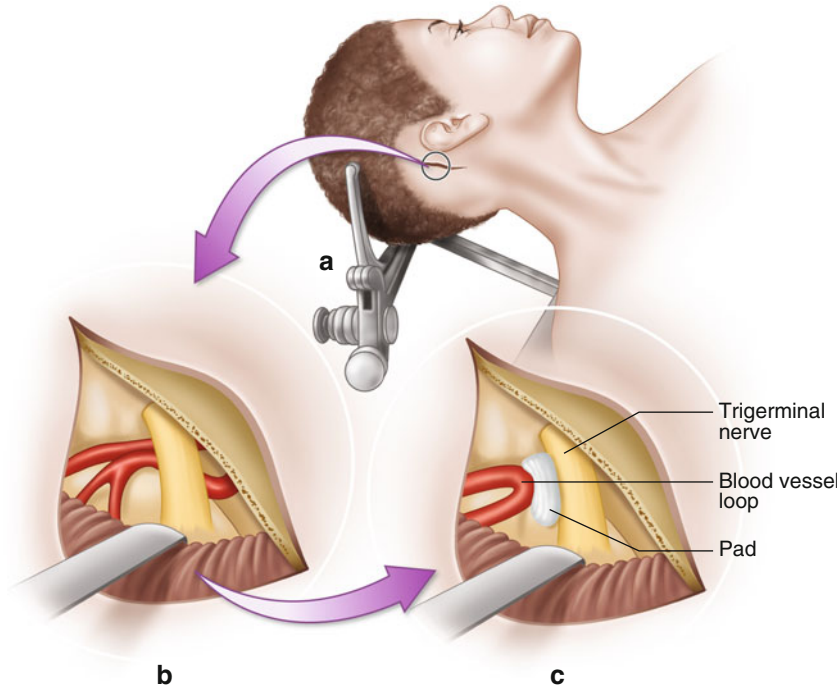

Fig. 14.2 Microvascular decompression. (**a**) Access to the trigeminal or facial nerve is accomplished through a posterior fossa craniotomy. (**b**) The cerebellum is retracted exposing the nerve and the offending blood vessel. (**c**) A Teflon pad is placed between the nerve and vessel, decompressing the nerve

for chewing. The trigeminal nerve has three major branches. The ophthalmic, or upper, branch supplies sensation to most of the scalp, forehead, eye, and eyebrow. The maxillary, or middle, branch passes through the cheek, upper jaw, top lip, teeth and gums, and to the side of the nose. The nerve's mandibular, or lower, branch passes through the lower jaw, teeth, gums, and bottom lip. More than one nerve branch can be affected by the disorder. The superior cerebellar artery (SCA) is the vessel most often responsible for neurovascular compression of the trigeminal nerve root, although other arteries or veins may be the culprit vessels [1]. BAEPs and EMG for CNV and CNVII are typical modalities used for monitoring of MVD to relieve trigeminal neuralgia. The t-EMG response for CNV can easily be confused with CNVII responses. The latency of a t-EMG response from the trigeminal nerve should be around 5 ms, while a facial nerve response is seen around 7 ms when stimulated near the exit point from the brainstem.

Hemifacial spasm (HFS) is characterized by intermittent, involuntary twitching of the muscles in one side of the face, which lasts from a few seconds to several minutes. Spasms occur spontaneously and without warning. They are often exacerbated by stress or fatigue but can also be triggered by stimuli like sunlight, touch, chewing, and talking. Spasms do not cause pain, but can cause discomfort, impaired vision, social distraction, and embarrassment. HFS is most often caused by a branch of the posterior inferior cerebellar artery (PICA) or anterior inferior cerebellar artery (AICA), pulsating against the facial nerve root as it leaves the brainstem resulting in hyperactivity of the facial nerve [1, 2]. Similar to the treatment for trigeminal neuralgia, to relieve HFS symptoms, the facial nerve must be moved away from the offending vasculature.

To adequately monitor the facial nerve, electrodes are placed in muscles corresponding to the extracranial branches that control facial expression. For example, electrodes can be placed in the orbicularis oculi (temporal branch), nasalis (zygomatic branch), orbicularis oris (buccal branch), mentalis (mandibular branch), and if requested, the platysma (cervical branch). Free-running EMG responses in any of these muscles can indicate surgical manipulation [3]. Triggered-EMG responses can assist the surgeon in verifying the degree of decompression of the nerve. In patients with HFS, stimulation of a branch of the facial nerve may result in delayed muscle activity recorded from myotomes of adjacent branches. This is known as a lateral spread response. Current understanding is that compression of the nerve causes antidromic signals to travel back to the facial nerve nucleus within the brainstem where the nucleus becomes hyperactive and sends signals to all branches, resulting in abnormal facial movements [2–5]. Stimulation of a branch of the facial nerve may have the same effect. For example, stimulating the marginal mandibular branch and seeing a delayed response in the orbicularis oculi is evidence of a lateral spread response (Fig. 14.3). Once the offending vessel is isolated and adequate decompression has been achieved, this abnormal muscle response usually disappears. If it still persists, an additional vessel that was not apparent during visual inspection may be compressing the nerve. Monitoring the lateral spread response decreases the incidence of reoperation.

The close proximity of CNVIII puts hearing at risk during surgery for MVD. BAEPs during HFS surgery to protect hearing. In addition, BAEPs offer protection against ischemia to the brainstem.

Vestibular Schwannoma

A vestibular schwannoma, also referred to as an acoustic neuroma, is a benign slow growing tumor that arises from the Schwann cells covering the vestibulocochlear nerve. The vestibulocochlear nerve is the eighth cranial nerve (CNVIII) and is a sensory nerve that facilitates hearing and balance. Symptoms caused by a vestibular schwannoma correlate with the size and growth of the tumor. The most common early symptom is hearing loss. Small tumors can cause hearing loss, tinnitus, and dizziness. As the tumor expands into the cerebellopontine angle—the anatomic space between the cerebellum and the pons—hearing loss may worsen, facial weakness

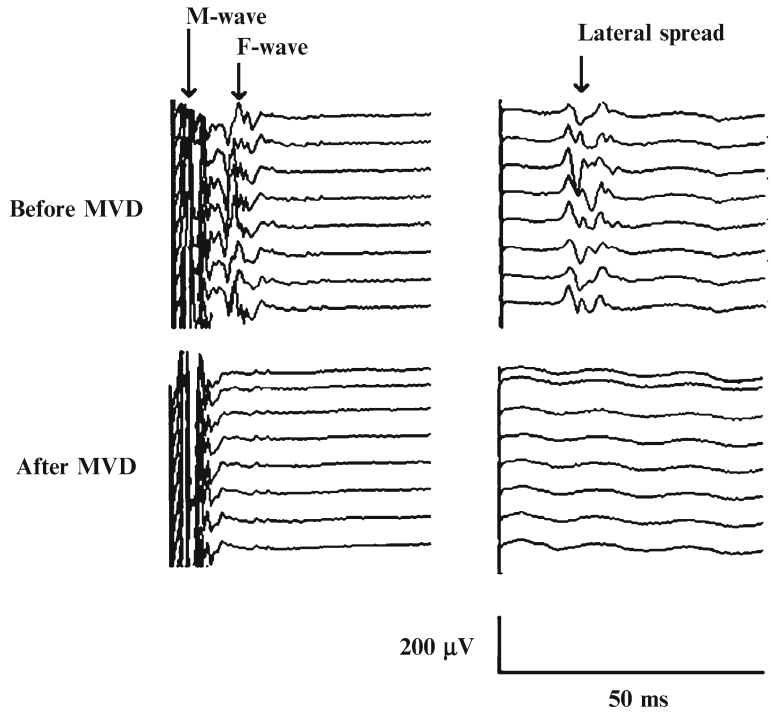

Fig. 14.3 Recordings of LSR and F wave were obtained after direct stimulation of marginal mandibular branch (*left column*) showing LSR to the orbicularis oculi muscle (*right column*). Simultaneous disappearance of the LSR and F wave after MVD was achieved. From Fernández-Conejero I, Ulkatan S, et al. Intra-operative neurophysiology during microvascular decompression for hemifacial spasm. Clin Neurophysiol. 2012;123:78–83

can occur, and balance problems may worsen. Large tumors can compress the brainstem, with severe compression causing all of the above symptoms as well as headaches and visual problems [6]. While small tumors or those causing few symptoms can be observed, surgical removal is the most common treatment for large tumors. The goal of surgery is to (1) maintain facial nerve function, (2) preserve socially useful hearing in the affected ear, and (3) remove as much tumor as possible. Total tumor removal carries a higher risk of hearing loss and facial nerve damage so surgeons often opt for partial or near-total tumor removal in order to preserve neurological function [7].

There are three main approaches to remove a vestibular schwannoma from which the surgeon can choose based upon tumor size, location, and hearing status [8]. With a suboccipital (retrosigmoid) approach, an incision is made behind the ear and through the occipital bone to expose the internal auditory canal and the tumor. With a translabyrinthine craniotomy, the approach is through the ear in the mastoid bone. The semicircular canals are removed to expose the tumor resulting in complete sensorineural hearing loss in the ipsilateral ear. A middle fossa approach is above the ear in the temporal bone, exposing the internal auditory canal and the tumor. This approach can be used for small tumors and when hearing preservation is optimal.

During any of these approaches, the use of intraoperative monitoring can further assist the surgeon in locating and protecting cranial nerves. Surgeons often choose to utilize EMG for CNVII to protect from surgical manipulation damage to the nerve or if the facial nerve is being directly affected by the tumor. A very large tumor may require EMG for CNV as well. Once the tumor is removed, the integrity of the facial nerve can be tested by electrically stimulating at points proximal and distal to the site of tumor resection. A good prognosis for facial nerve function is if low-intensity proximal and distal muscles responses

are the same [9]. Additional studies suggest a low threshold response of 0.05 mA or lower with response amplitudes >240 μV is indicative of preserved facial nerve function [10, 11].

CNVIII is monitored using BAEPs, not only watching the risk to the nerve associated with stretching or compression but also detecting changes in the function of the brainstem. With a translabyrinthine approach, hearing is sacrificed but monitoring BAEPs on the contralateral side can help protect brainstem integrity. According to Angelo and Møller, recording of the BAEP makes it possible to detect insults to the brainstem before changes in cardiovascular function become apparent [12].

Chiari Malformation

A Chiari malformation (CM) is a condition in which the cerebellum herniates through the lower part of the skull and down into the spinal canal. The herniated tissue compresses the brainstem and blocks the normal flow of cerebrospinal fluid (CSF). The blockage can cause an irregular flow and build up of fluid in the spinal cord. This can cause CSF the formation of a fluid-filled cavity in the surrounding white matter to accommodate the backed up CSF. Such a cavity is called a syrinx, and the condition is known as syringomyelia (Fig. 14.4). Chiari malformations are found in both children and adults and are often difficult to diagnose. Symptoms can be variable from one patient to another and are not always related to the size of the herniation. Treatment options depend on the type of malformation and the severity of the symptoms, which can range from headaches, neck pain, and vertigo to numbness in extremities, vision problems, hearing loss, fatigue, and depression.

If symptoms worsen or medications are no longer effective, a posterior fossa decompression may be necessary to create room for the cerebellum and the brainstem.

There are four grades of Chiari malformations (CMI–CMIV). In CMI, symptoms usually appear during later childhood or early adulthood. CMII is discovered during pregnancy or at birth and is almost always accompanied by a form of spina bifida called myelomeningocele, where the backbone and spinal canal have not closed properly [13]. CMIII and CMIV are the most severe and are discovered at birth or with intrauterine ultrasound. This section discusses only the pathology of Chiari malformation type I.

Beyond the cerebellar tonsils being displaced, a high incidence of patients with CMI will develop syringomyelia, which can cause irreversible damage to the spinal cord [14]. In addition to symptoms resulting from the cerebellar herniation, a patient's myelopathic symptoms may be attributed

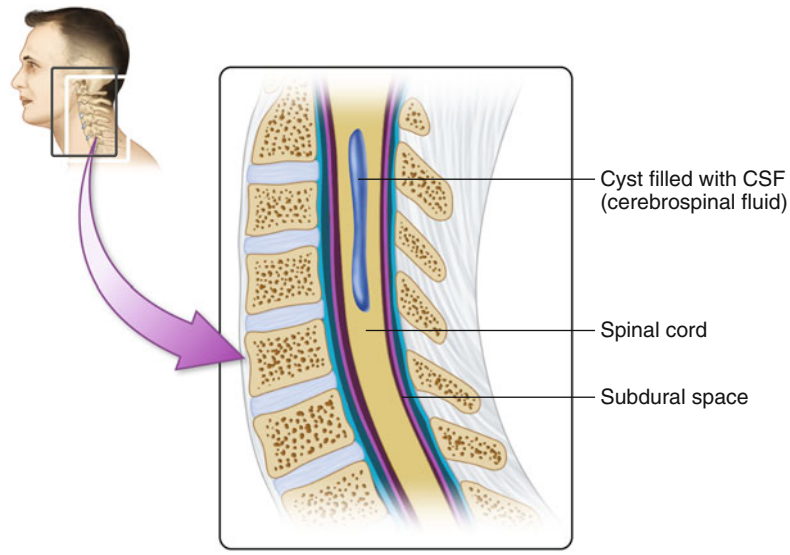

Fig. 14.4 Syrinx

to an expanding syrinx. Compression of the brainstem and cranial nerve nuclei can occur as well leading to issues with sleeping, breathing, facial pain and numbness, and hearing loss.

In order to stop the progression of the herniation or if symptoms are worsening, a posterior fossa decompression is performed to reduce pressure on the cerebellum and spinal cord and restore the normal flow of CSF. An incision is made down the back of the neck, exposing the skull and the top of the spine. A suboccipital craniotomy removes a small section of the skull. A C1 laminectomy may also be required for full decompression. Bony decompression will relieve pressure on the herniated tissue, but to fully restore CSF flow, the dura may need to be opened and then replaced with a larger autologous or synthetic dural patch. Shunting of the syrinx may also be necessary to drain CSF and relieve compression of the spinal cord.

Multiple structures and neurological functions can be at risk during surgery for a Chiari malformation. IOM is typically chosen to protect the brainstem, cerebellum, and spinal cord. As with other posterior fossa surgeries, BAEPs are used to monitor the integrity of the brainstem and effects of retraction on the cerebellum. The ascending and descending pathways of the spinal cord and brainstem are also at risk. The use of somatosensory evoked potentials (SSEPs) and transcranial motor evoked potentials (TcMEPs) will provide protection for the dorsal column pathway as well as the corticospinal tract as they pass from the brainstem into the spinal cord.

Conclusion

It is an understatement to say that multiple vital structures are in close proximity to one another in the posterior fossa. The anatomy of this area may also be very complex, and these vital structures can be difficult to identify, especially if a tumor has altered the anatomy even further. Neurosurgical procedures of the posterior fossa can involve the cranial nerves, brainstem, cerebellum, and the spinal cord. The use of multimodality IOM—using EMG and evoked potentials—assists the surgical team in identifying structures at risk, as well as verifying structural integrity at the close of the procedure.

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Intraoperative Monitoring for Carotid Endarterectomy

15

Scott Francis Davis and Jeremy Andrew Bamford

Carotid endarterectomy (CEA) is the most frequently performed procedure for the prevention of stroke. Strict selection criteria are applied to determine surgical candidates for CEA as indicated for the treatment of moderate to severe carotid stenosis. Carotid endarterectomy is associated with procedural and periprocedural risks including stroke (embolic or hemodynamic), myocardial infarction, as well as cranial nerve palsy resulting from traction on the recurrent laryngeal nerve. Recent attention has turned to a less invasive surgical approach to treat carotid stenosis, carotid stenting. Stenting and endarterectomy have shown comparable efficacy, but more randomized studies are needed [1].

Carotid revascularization by endarterectomy involves clamping the common, external, and internal arteries so that the vessel can be incised and the plaque removed. The ability of the patient to tolerate the cross-clamp depends on the sufficiency of collateral flow through the circle of Willis. Prior to routine intraoperative monitoring of cerebral perfusion, the surgeon would place an intraluminal shunt in all patients for the purposes of maintaining blood flow around the clamp. Routine shunting has been largely abandoned in favor of selective shunting [2–5]. In selective shunting, the need for a shunt is determined by intraoperative electrophysiological monitoring data [6]. The incidence of procedural embolic stroke is possibly correlated with the use of intraluminal shunts [4, 7]. This could be explained by increased chance of introducing particulate emboli when the shunt is inserted through a diseased arterial wall. However, the literature is not in agreement that selective shunting reduces intraoperative stroke complications over routine shunting and more randomized studies are called for [8]. The monitoring community, nevertheless, advocates selective shunting, because the need for a shunt can be determined with high sensitivity and specificity with the use of electrophysiological monitoring methods. In addition, continuous monitoring can detect ischemic changes during other critical phases of the procedure as well as monitor the function of an intraluminal shunt if placed. In order for selective shunting to be safely performed, a means for assessing collateral flow and monitoring ongoing cerebral perfusion must be utilized. Older methods of monitoring, such as measurement of carotid stump pressure and cerebral oximetry, have either been replaced or become adjunct to the modalities of EEG and median nerve SSEP [9–12]. Transcranial Doppler studies may be added to monitor for particulate

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emboli associated with clamp release and reperfusion as well as intraoperative ischemia [13–15].

It is essential that the neuromonitorist understand the critical phases of the endarterectomy procedure and the risks associated with each phase. Determining the likely cause of intraoperative changes, such as whether a stroke is embolic or hemodynamic in nature, is critical to providing relevant information that may be used by the surgeon or anesthesiologist to formulate an intraoperative treatment plan and prevent a negative outcome.

Intraoperative monitoring of CEA should include multiple modalities including EEG and median nerve SSEP [16, 17]. Continuous monitoring is advised even once a shunt has been placed as the integrity of the shunt may fail and go undetected by the surgeon. An appreciation for the endarterectomy procedure is necessary to insure appropriate attention is paid to all times of increased risk of neurological injury as complications are not restricted to clamping [18]. Both technical and professional monitoring personnel must be well trained and familiar with alarm criteria as well as recording parameters for monitored modalities.

Carotid Stenosis

Stroke is one of the leading causes of death and disability in the United States, and carotid stenosis is one of the leading causes of stroke [19]. Stenosis can occur in any artery in the body and is a result of the accumulation of atherosclerotic plaque buildup on the arterial wall. The most common sites for stenosis are arterial bifurcations. At an arterial bifurcation, blood flow is turbulent and there is more opportunity for plaque accumulation. A good analogy for this process is a fork in a river. The fork is the point along the course of a river where you are most likely to encounter "white water" and find debris along the riverbanks. Carotid stenosis occurs most often at bifurcation of the common carotid into the internal and external carotid arteries (Fig. 15.1).

Carotid endarterectomy is the surgical option for treatment of carotid stenosis. Stenosis that occurs much higher near the intracranial segment of the internal carotid artery cannot be treated with endarterectomy, and carotid artery stenting must be considered [20].

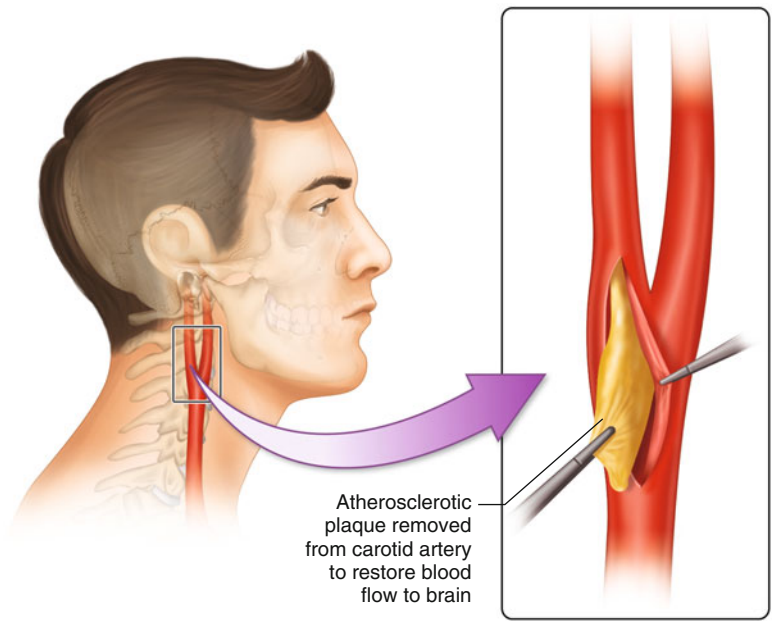

Fig. 15.1 Drawing showing the carotid bifurcation and the removal of plaque at this site by endarterectomy

Selection Criteria for CEA

Carotid endarterectomy carries with it the risk of stroke and death along with the risks associated with general anesthesia [21–23]. For this reason the risk to benefit ratio should favor surgical intervention. Recent studies have led to strict selection criteria for patients undergoing CEA. Current selection criteria support CEA for symptomatic patients with severe (>70 %) and moderate (50–69 %) stenosis as well as asymptomatic patients with severe stenosis. Other factors taken into consideration include comorbidities that may increase the perioperative complication rate, history of ipsilateral stroke, and life expectancy [24–26].

Preoperative Testing

EEG and SSEP testing may be performed on a patient prior to the day of surgery. This is not required for accurate intraoperative neurophysiological monitoring of the patient but may be useful in determining whether any abnormalities or asymmetries may be expected in the operating room. The existence of preoperative asymmetries should heighten the awareness of the monitorist of an increased potential for change during cross-clamping especially if there are any residual neurological symptoms following a prior stroke [27]. It is important to utilize the results of preoperative testing for the purposes of planning while remembering that the patient's intraoperative (post-induction) baselines will be the only data that matter during the monitoring procedure.

Anesthesia for Monitoring of CEA

The anesthetic regimen for intraoperative neurophysiological monitoring of any surgical case is determined based on the modalities to be monitored. For monitoring of most endarterectomies, the anesthetic requirements for SSEP and EEG recordings are to be considered [28]. Anesthesia and intraoperative monitoring is reviewed elsewhere in this volume. When monitoring of the recurrent laryngeal nerve is included in the monitoring protocol, the avoidance of muscle relaxants would also be essential. In the absence of preoperative EEG and SSEP testing, a preinduction baseline can illuminate any asymmetries due to a prior ischemic event. No further importance should be given to preinduction data, as the post-induction baseline will be the data against which changes are judged.

The pattern of EEG will change as the patient proceeds through the various states of anesthesia [28, 29]. Rapid induction, especially with barbiturates, will result in an alpha/beta pattern dominant in the frontal channels. As the stage of anesthesia moves toward the surgical plane, this activity will generalize and then begin to slow. Increases in volatile anesthetics beyond 1 MAC may result in a burst suppression pattern in the EEG, which is not conducive to monitoring EEG. If the EEG is in burst suppression, it is important for the monitoring team to inform the surgeon that EEG monitoring is currently unreliable and then begin to work with the anesthesia team to adjust the regimen to one more permissive of EEG monitoring. Anesthetic protocols may involve the use of minimal inhalants with the addition of a propofol infusion. In many instances it is preferable to have the volatile agent higher as long as it does not exceed 1 MAC and the propofol infusion rate lower. It would be better to avoid a propofol infusion altogether since propofol can lead to a concentration-dependent burst suppression of the EEG. While it is optimal to have data from multiple modalities available when making interpretations, it is worth noting that SSEPs can still be reliably monitored even when the EEG is in burst suppression [30, 31]. Good communication with the anesthesia team prior to the case will help insure that such interruptions in monitoring are kept to a minimum.

Changes in the anesthetic load will also affect the reliability of SSEP data. Symmetric changes in the cortical potential (N20) can be suggestive of anesthetic change, but the possibility of a surgical or peri-surgical cause cannot be ruled out. An asymmetric reduction in the amplitude or latency increase of the N20, however, is suggestive

of a clinically significant change over an anesthetic-induced change. It is important that the anesthesia team be aware that changes in anesthetic load (e.g., delivering a bolus) are undesirable, especially near the time of or during an important surgical step.

Monitoring the patient's physiological status is an important job of the anesthesia team. The neurophysiological monitoring clinician can aid the anesthesia team by correlating change in physiological status with cerebral perfusion. One of the most important functions of the anesthesia team during the procedure is regulation of the mean arterial pressure (MAP). Unlike most spine procedures, the CEA requires that the patients MAP be carefully regulated at different points during the procedure [32]. For example, the MAP is increased during clamp to facilitate collateral circulation but reduced just before unclamping to avoid reperfusion injury. In addition, many patients undergoing CEA have a history of cardiovascular disease and hypertension, which may impede the ability of the arterial system to autoregulate. The consequence of this is that the patient may not tolerate the mean arterial pressure that they are being maintained at by the anesthesia team. Changes in neurophysiological data not correlating with a surgical step may be a result of changes in MAP. This becomes even more critical during both clamping and reperfusion (clamp release) when MAP must be carefully regulated.

Procedure Details and Critical Phases for Monitoring

While continuous neurophysiological monitoring is essential, there are critical phases of the procedure that warrant specific consideration due to the increased risk (Fig. 15.2). Thompson and Talkington [32] provide a good review of the procedural details of carotid endarterectomy. For the purposes of intraoperative monitoring of the procedure, it is important that the monitorist establishes quality baseline data for all modalities monitored after induction but well before cross-clamp. Premedicated baselines should be

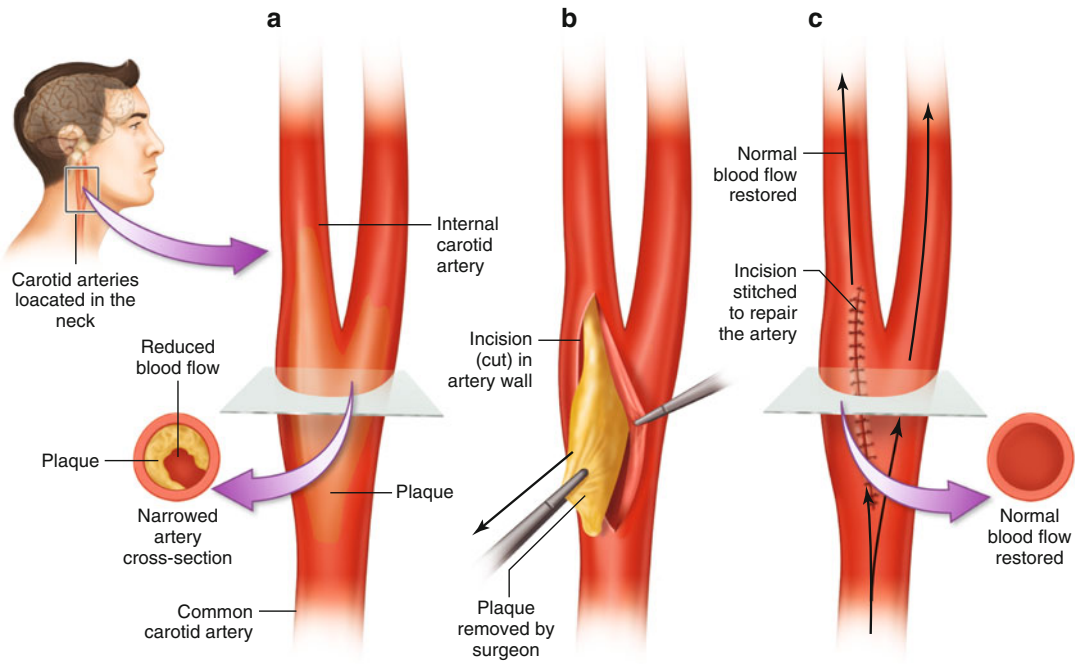

Fig. 15.2 The surgical steps of carotid endarterectomy

considered when possible solely for the purposes of revealing any preoperative asymmetries. At least a post-induction 10-min pre-clamp baseline should then be established for the purposes of comparing testing results throughout the procedure [33].

The first critical event is administration of heparin. Heparin, an anticoagulant, is given prior to carotid cross-clamp for the purpose of preventing thrombus formation that may lead to embolic stroke on reperfusion. By the same mechanism, heparin may re-aggravate any bleeds that may have occurred from aneurysms or other disorders. It takes 4–5 min on average for heparin to raise the active clotting time sufficiently to proceed with carotid cross-clamping.

The next critical event, carotid artery cross-clamping, is likely the reason the surgeon has ordered monitoring to begin with. As you recall, the carotid arteries feed the ipsilateral anterior circulation of the brain. In most healthy patients, the contralateral circulation compensates for loss of blood flow from one carotid artery. This compensation occurs by virtue of collateral circulation through the circle of Willis. A majority of people have an incomplete circle of Willis, of which there are many variants (Fig. 15.3) [34]. Although incomplete, the circle of Willis is still adequate to provide sufficient collateral circulation in most people. There are, however, certain anatomic variants or pathological conditions (including prior stroke) that result in the inability of the contralateral circulation to compensate for a unilateral carotid occlusion such as occurs during carotid clamping [35]. Changes in electrophysiological data that correlate with carotid cross-clamping should be taken as an alarm that collateral circulation is inadequate to perfuse the brain. A further discussion of alarm criteria will be presented below. In order to facilitate endarterectomy, the common, external, and internal carotid arteries must all be clamped. When collateral circulation is judged inadequate by changes in electrophysiological data, the surgeon will place an intraluminal shunt whose purpose is to reroute blood around the clamp maintaining flow to the brain. Due to the increased risk of embolic stroke with shunt placement, the current standard is to shunt selectively

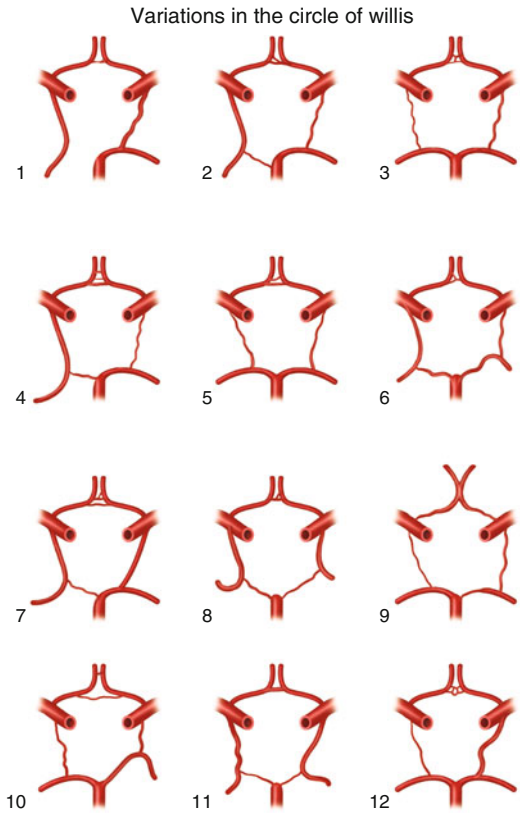

Fig. 15.3 Illustration of 12 variations seen in the circle of Willis

as determined by changes in the monitoring data [4, 6, 7]. The anesthesia team must carefully manage the patient's blood pressure during cross-clamp. In order to support collateral circulation, the blood pressure is elevated above normal pre-clamp levels. Sufficient blood pressure can be titrated by carefully observing electrophysiological data from SSEPs and the EEG. Insufficient perfusion will result in a loss of amplitude from recorded signals providing a functional assay that can be used to determine the best blood pressure for the patient.

While carotid cross-clamping is largely considered the most critical phase of the endarterectomy procedure by many, reperfusion is the phase during which the patient is most at risk of suffering a stroke. When the carotid cross-clamp is released, particulate emboli are released into the circulation. Most of these emboli are too small to

cause a problem, but occasionally larger emboli may become lodged in a smaller vessel creating an obstruction [36]. If the obstruction occurs in a cerebral vessel, the resulting ischemia will likely be detectable as a change in SSEP or EEG data prompting intervention. A subcortical obstruction, however, will likely go undetected by routine monitoring modalities. Figure 15.4 shows an example of a clamp-related change in SSEP and EEG data and recovery of these data following insertion of an intraluminal shunt.

Reperfusion injury may occur secondary to a condition known as cerebral hyperemia [37]. Hyperemia can happen in any organ and is the result of too much blood flow. Hyperemia commonly known as reactive hyperemia may occur after a period of ischemia, which, in the case of CEA, may occur during carotid cross-clamp [38]. Hyperemia may develop in the postoperative period and occasionally develops intraoperatively sometime after clamp release. The increase in blood flow seen in hyperemia may cause an increase in intracranial pressure (ICP) that can compress the brain resulting in injury. Transcranial Doppler is the most useful modality in detecting postoperative hyperemia.

EEG Monitoring

Continuous EEG monitoring is used intraoperatively to assess the adequacy of cerebral perfusion and help determine the need for a shunt during carotid endarterectomy [39]. Intraoperative EEG monitoring for carotid endarterectomy does not necessitate recording as many channels as diagnostic EEG. A minimum of eight channels is required for intraoperative monitoring, while the use of more channels is encouraged [40]. The generator of the EEG signal is the cerebral cortex, and as such only cortical perfusion may be monitored with this modality. Subcortical events, such as embolic stroke, are unlikely to be detected with EEG.

EEG monitoring has the advantage of allowing direct monitoring of cerebral function as opposed to modalities such as stump pressure or TCD that only provide an indirect measure of cerebral function. Only SSEPs have demonstrated equal sensitivity to EEG [16]. The addition of median nerve SSEPs, thus, provides a necessary redundancy to EEG monitoring. Hemodynamic changes that do not affect the EEG can usually be assumed to be clinically insignificant, unless an effect is seen in the SSEP recording. EEG monitoring has largely replaced cerebral oximetry for carotid monitoring; however, oximetry may still be used as an adjunct in some centers. Cerebral oximetry measures regional oxygen saturation from the frontal lobes and primarily samples venous blood [9, 11, 12]. The effect of changes in oximetry on cerebral function must be inferred in contrast to the direct information provided by EEG. The following sections provide technical information on setting up and running the intraoperative EEG for monitoring a carotid endarterectomy. The reader is encouraged to become familiar with professional practice guidelines and position statements [41, 42].

Electrode Placement

Stainless steel subdermal needle electrodes are most commonly used for intraoperative EEG with some centers still opting for cup electrodes. The use of needles facilitates a safe and efficient recording setup without the use of adhesives. Electrodes should have an impedance of less than 5 kΩ. A minimum of eight channels of EEG should be recorded for monitoring of carotid endarterectomy. There are several acceptable montages for EEG monitoring of CEA. Table 15.1 shows one of the more commonly used montages often referred to as the modified double banana. A referential montage refers all active leads to a common cephalic reference (usually Cz). In a bipolar montage, active leads are referenced to each other giving the added advantage of increased specificity or ability to more easily locate the area of change. Since efficiency is required in the operative setting, many monitorists make use of their SSEP scalp leads in their EEG montage. The most important considerations are that the choice of recording sites contains areas from frontal to occipital and that leads are placed symmetrically on the left and right side.

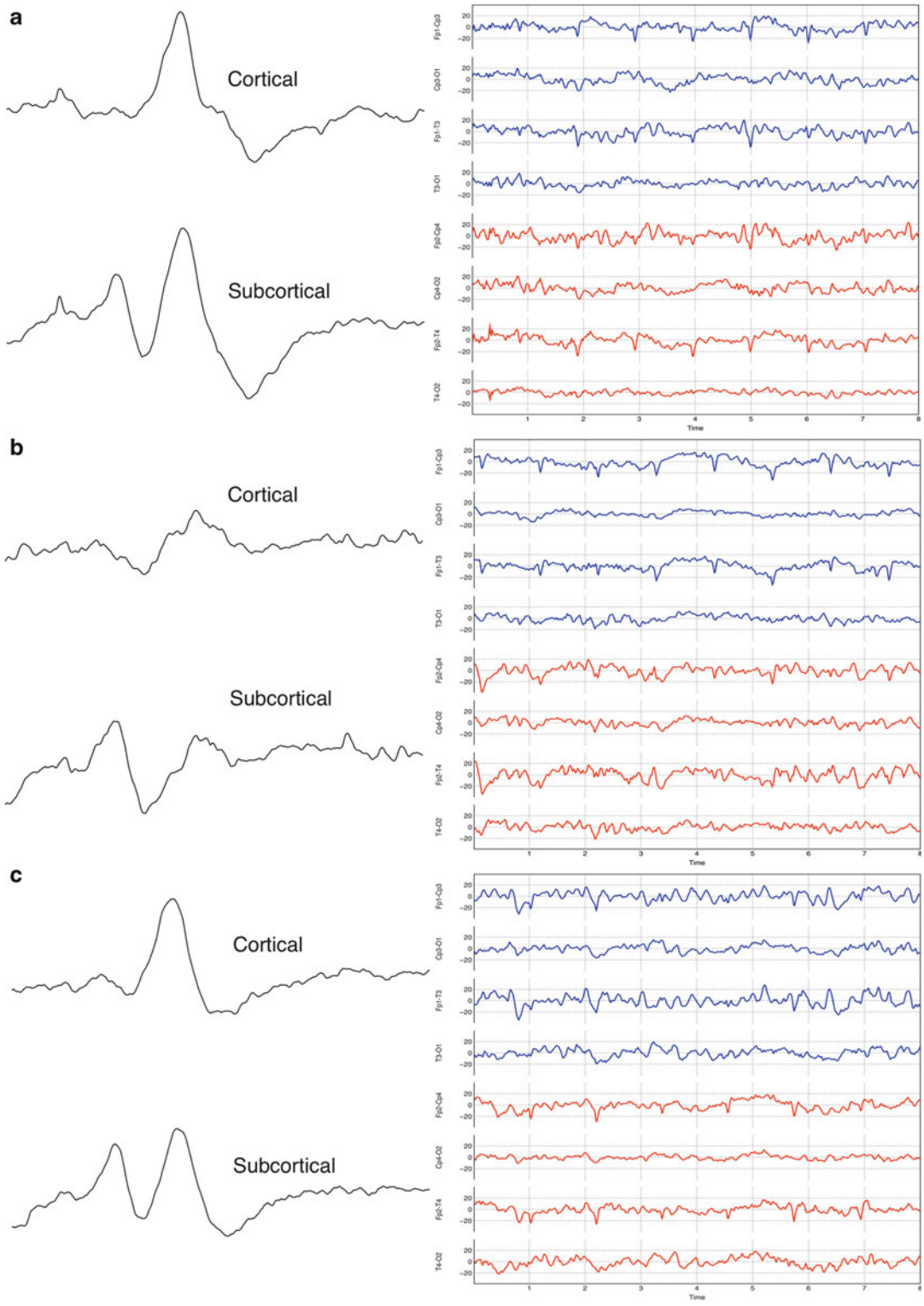

Fig. 15.4 Clamp-related SSEP and EEG change (**a**) SSEP and EEG baseline data established prior to carotid cross-clamp. (**b**) Data taken immediately after carotid cross-clamp showing amplitude reductions in the left cortical SSEP and left EEG. Note no change in the subcortical SSEP data. The generator of this potential is supplied by the posterior cerebral circulation. (**c**) Data taken after shunt placement showing recovery of all amplitudes

Table 15.1 Modified double banana electrode placement

Left	Right
Fp1-Cp3	Fp2-Cp4
Cp3-O1	Cp4-O2
Fp1-T3	Fp2-T4
T3-O1	T4-O2

Recording Parameters

Intraoperative EEG recording should have a bandpass of 0.5–70 Hz. Higher frequency signals such as the gamma band are not seen intraoperatively since they are associated with cognitive function. A notch filter may be used, but only when all attempts at eliminating the source of 60 cycle noise have failed.

Sweep speed (time base) may be set according to the preference of the monitorist with equivalent paper speeds of 10–30 mm/s being the most common. Shorter time bases make it easier to detect changes in the fast beta activity. This activity is generally the first to disappear in an ischemic event.

Sensitivity should be set such that the waveforms are not clipped (sensitivity too high) or appear to flat (sensitivity too low). Intraoperative EEG is generally of lower amplitude than diagnostic EEG and thus is best viewed between 30 and 50 μV/cm.

Analyzed EEG

The advent of digital EEG has led to the ability to instantly analyze the raw EEG waveform and represent the composite waveform as a spectrum of its component frequencies. This type of analysis is termed spectral analysis and is accomplished with a fast Fourier transform (FFT) algorithm. To perform spectral analysis, the raw EEG waveform is sampled at a desired rate that is set by the user. The composite waveform (sample) is deconstructed into its component frequencies using FFT. The results are displayed graphically showing the power of each frequency band in the composite signal.

Spectral analysis can be useful during a carotid endarterectomy to confirm suspected changes in frequency detected by visual interpretation of raw EEG. It is important to note that the analyzed EEG is not a substitute for the raw EEG and that the raw data should be used as the primary source for interpretation [43].

Alarm Criteria

Alarm criteria for EEG are not widely agreed upon. Correlating different degrees of EEG changes with postoperative outcome and assigning weight to the type of change (amplitude reduction, general slowing, reduced fast activity, etc.) is problematic. One commonly used set of criteria include a 50 % or greater reduction in amplitude associated with slowing. When less significant changes are judged to be clinically significant, the specificity of the EEG decreases. In spite of the possibility of decreased specificity, it is reasonable to take as clinically significant any change that correlates with a critical surgical event (such as clamping). Future studies may better define safe windows for change. Most clamp-related changes in the EEG recording occur within the first 20 s in most patients with the remainder of patients showing changes within the first minute. Occasionally clamp-related changes may be seen as late as 4 min post-clamp. There are data correlating changes in analyzed EEG with postoperative outcome; however, one should be cautioned about using analyzed EEG to predict outcome in most practical settings.

SSEP Monitoring

The use of median nerve SSEPs have become a standard adjunct to continuous EEG monitoring during carotid endarterectomy. While MN-SSEPs provide specific protection to somatosensory cortex, they have demonstrated remarkable sensitivity to cerebral ischemia resulting from carotid cross-clamp. It has been argued that SSEPs are even more sensitive to ischemia than EEG.

The ease of SSEP interpretation compared with that of EEG may result in fewer missed occurrences when monitored by personnel less comfortable with EEG interpretation. Such events cannot be attributed to a failure of EEG monitoring, but rather interpretive error.

Stimulation Parameters

Adhesive surface electrodes are predominantly used for stimulation of the median nerve. Placement of the stimulating electrodes is between the tendons of the palmaris longus and flexor carpi radialis muscle (approximately 2 cm proximal to the wrist crease). Care should be taken to make sure the cathode (stimulating pole) is proximal to the anode in order to prevent the phenomenon of anodal blocking. In rare instances subdermal needle electrodes may be used when there is a patient history of peripheral neuropathy, body habitus, or adema.

A square-wave monophasic pulse with a pulse width of 200–300 μs is used as the stimulus. The pulse should be delivered at a frequency of approximately 3–5 pulses per second, taking care that the exact frequency is not divisible evenly by 60 so as not to average in line noise. The intensity of stimulation should be supramaximal. To titrate the supramaximal intensity, the current is increased stepwise until no additional increases in the amplitude of the response are measured and then 10 % is added to this intensity.

Recording Parameters

Median nerve SSEPs are recorded using a peripheral, subcortical, and cortical channel. The peripheral potential is recorded with the active electrode in the ipsilateral Erb's point and referenced to the contralateral Erb's point. The resulting signal is a peak of negative polarity and a latency near 9 ms. The generator is the brachial plexus. The N9 is most useful in determining the adequacy of stimulation as well as for monitoring the brachial plexus for positional issues. The subcortical (often called cervical) potential is recorded with an electrode usually placed around the C5 vertebrae. Alternate active electrode sites include over the mastoid bone, the earlobe, and the chin. The negative peak recorded at 13 ms and the corresponding trough at 14 ms are generated by the dorsal column nuclei and caudal medial lemniscus respectively. These potentials, similar to the N9, are not effected by anesthesia and are located caudal to the tissue at risk. The cortical potential is of greatest interest during a CEA. It is most commonly recorded with the active electrode at Cpc referenced to Fpz. Some monitorists prefer a non-cephalic reference such as the contralateral Erb's point if the fast frontal EEG commonly recorded from Fpz becomes problematic. The N18 is another peak of interest. Generated by the thalamus, this peak is recorded with the active electrode at Cpi referenced to the contralateral Erb's point. The thalamic potential is supplied by the posterior circulation. Monitoring this thalamic potential may be useful in detecting ischemia resulting from the phenomenon of posterior steal where too much blood is provided to the anterior circulation from the circle of Willis at the expense of posterior perfusion.

Alarm Criteria

Alarm criteria for SSEP monitoring are well agreed upon in general. For spinal cord monitoring the widely accepted alarm criteria are a 50 % reduction in amplitude and/or 10 % increase in latency. Lam et al. [16] found that a reduction of 50 % or greater in amplitude proved as sensitive as EEG monitoring for monitoring carotid endarterectomy. Similar to EEG changes, a minor or moderate change in SSEPs may or may not indicate an impending neurological deficit. It is clear that if minor SSEP changes are taken as an alarm, the overall specificity of SSEP monitoring will decrease significantly (more false positives). Until more research is done to define the significance level for SSEP monitoring for carotid surgery, many monitorists are more conservative with their approach to alarm criteria and report any change that correlates with a surgical event such as clamping or unclamping as significant.

Conclusions

Carotid endarterectomy is becoming one of the most commonly monitored surgical procedures. There are many opportunities for ischemic injury during the procedure, and the surgical and anesthesia teams must walk a fine line when regulating mean arterial pressure throughout the various phases of this surgery. Prior to the advent of patient monitoring, surgeons would place an intraluminal shunt in every patient. As it became evident that the use of a shunt increases the risk of an embolic stroke, surgeons began to look for ways to select patients for shunting based on adequacy of collateral flow. Initial techniques used for this purpose were limited to measuring carotid stump pressure during clamping and possibly continuous monitoring of cerebral oximetry. Neither of these modalities provides both a continuous and direct measure of cortical function during surgery. Later on, intraoperative EEG became standard protocol for monitoring CEA. The addition of neurophysiological monitoring to the procedure provides assurance to the surgeon that the brain is being adequately perfused during the entire procedure. Although the sensitivity and specificity of EEG monitoring is quite good, many intraoperative monitorists lacked formal training in EEG making them uncomfortable or unqualified to interpret real time EEG data for the purposes of assessing the adequacy of collateral flow. The addition of median nerve SSEPs to the monitoring protocol provided a familiar redundancy that could be used as an adjunct to EEG monitoring. With equal (if not greater) sensitivity and specificity to EEG, SSEPs have become a mainstay for intraoperative monitoring of carotid endarterectomy. Many centers now include transcranial Doppler monitoring to measure mean flow velocity in the middle cerebral artery and to detect emboli upon clamp release. The use of TCD for measurement of flow velocity does not provide the type of direct information on cortical function that EEG and SSEPs provide. In addition, the detection of emboli has not correlated well with clinical outcome.

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Monitoring ENT Procedures

16

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Monitoring for ENT Procedures

Intraoperative neurophysiological monitoring (IOM) is used during procedures of the head and neck. Procedures to remove tumors of the thyroid, parathyroid, and parotid glands put cranial nerves at risk, specifically the recurrent laryngeal nerve (RLN) (branch of CNX) and the facial nerve [1]. Electrophysiological testing and monitoring of the cranial nerves at risk accomplishes three goals: (1) to identify the nerve within the surgical field for the purposes of aiding the surgeon in avoiding damage to the nerve during the procedure, (2) to monitor the nerve during the course of the procedure in order to provide real-time feedback to the surgeon about the activity of the nerve, and (3) to provide the surgeon with a prognostic indicator of postoperative nerve function by assessing the stimulation threshold of the nerve at the end of the procedure [2]. These three goals of IOM for ENT procedures contribute to the overall mission of IOM to reduce the incidence of iatrogenic neurological injury. This chapter discusses practical applications of intraoperative monitoring for thyroidectomy, parathyroidectomy, and parotidectomy.

The Thyroid and Parathyroid Glands

The thyroid gland is one of the largest endocrine glands and is located in the anterior compartment of the neck inferior to the thyroid cartilage. The thyroid is a butterfly-shaped gland consisting of a right and left lobe connected by an isthmus (Fig. 16.1). Anteriorly, it is covered by the infrahyoid (strap) muscles, and posteriorly, the gland is attached to the cricoid cartilage (just inferior to the thyroid cartilage) and tracheal cartilage. This is why the gland actually moves during swallowing. The thyroid secretes hormones that help regulate the body's metabolism and affect the function of many other systems in the body. Located on the posterior surface of the thyroid are the parathyroid glands. There are typically four parathyroid glands, each about the size of a grain of rice, that are positioned in the upper and lower corners of the lobes on each side of the thyroid. The major function of the parathyroid glands is to maintain serum calcium levels; therefore, the parathyroid glands are often saved and explanted into surrounding tissue when a total thyroidectomy is performed.

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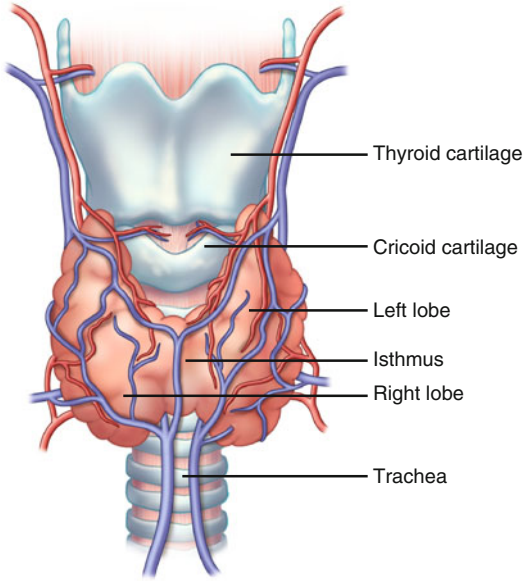

Fig. 16.1 The thyroid gland and surrounding structures

Thyroidectomy

Removal of the thyroid gland is indicated for a variety of conditions including tumor, goiter, or hyperthyroidism among others. Depending on the pathology, one (hemithyroidectomy) or both (total thyroidectomy) lobes may be removed. To access the thyroid and/or parathyroid glands, a horizontal incision is made across the front of the neck followed by a longitudinal incision through the strap muscles. Division of the local vasculature follows division of the musculature so that the lobes of the thyroid can be mobilized. RLN identification is the first goal of IOM for thyroidectomy. Identification of the RLN is essential for the purposes of avoiding the nerve during the procedure. Identification of the RLN is only assured when electrical stimulation results in a recorded compound muscle action potential (CMAP) from the vocalis muscle on the EMG recording.

The Recurrent Laryngeal Nerve

The RLN is a branch of the vagus nerve (CNX) that supplies motor function and sensation to the larynx. It innervates all of the intrinsic muscles of the larynx except the cricothyroid muscle, which is innervated by the superior laryngeal nerve (SLN). The RLN branches from the vagus nerve at the level of the subclavian artery on the right and the aortic arch on the left. After looping under the respective artery, the RLN ascends along the tracheoesophageal groove. The paired nerves are named "recurrent" because after branching, they turn back or run in a direction opposite to the vagus nerve. A minority of patients have a nonrecurrent laryngeal nerve branching off the vagus nerve at the level of the cricoid. During surgery, the RLN can be injured in a number of ways: complete or partial transection, traction, compression, misplaced ligature, thermal injury, or ischemia [3]. If the RLN is injured, it can result in temporary or permanent nerve paralysis. If the damage is unilateral, the patient may wake up with hoarseness. If there is bilateral nerve palsy, the airway may be compromised, resulting in dyspnea and in severe cases the need for a tracheostomy. The RLN also provides sensory innervation to the glottis, and a deficit may result in problems swallowing. Rates of injury range from 1 to 8 %, with significantly increased risk to the RLN when surgery is for reexploration, thyroid carcinoma, and total thyroidectomy [3–5]. In addition to thyroid and parathyroid procedures, the RLN is often monitored during ACDF, aortic arch procedures, carotid endarterectomy, and posterior fossa surgeries [6–8]. The SLN can also be injured during surgery [9, 10]. To monitor the SLN, the surgeon must place electrodes/needles in the cricothyroid muscle [9, 10]. Damage to the SLN results in a monotone voice or inability to change pitch.

RLN Monitoring

Spontaneous and triggered EMG recorded from the vocalis muscle is used to monitor the RLN. During thyroid and parathyroid procedures, it is imperative that two channels are available to monitor both the left and right vocal cords. Endotracheal (ET) tubes with left and right electrodes integrated directly into the tube are commercially available. Alternatively, adhesive paired

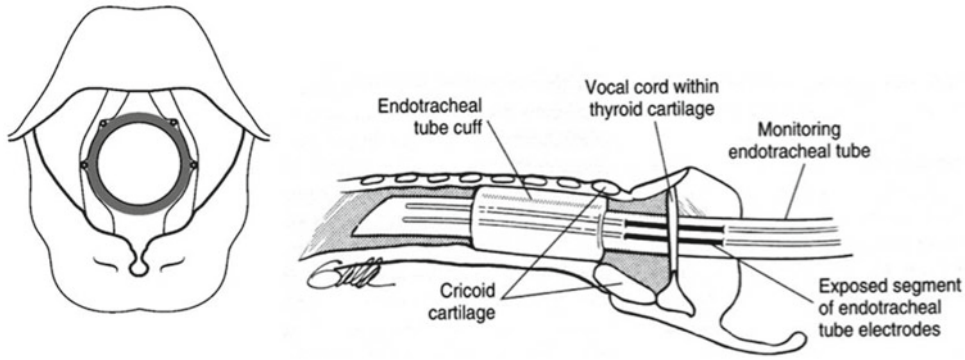

Fig. 16.2 Proper placement of endotracheal tube electrodes

electrodes can be attached to standard ET tubes. Proper placement of the electrodes of the endotracheal tube is of critical importance [2, 11, 12] (Fig. 16.2). Early communication with the anesthesia team will greatly aid in confirming proper electrode placement. The neuromonitorist should request a short acting paralytic for intubation such as succinylcholine as well as avoidance of lidocaine as these drugs will impair early recording ability for the purposes of confirming correct electrode placement [2]. Since the anesthesiologist will be placing the endotracheal tube with electrodes, the monitorist should be able to guide him in proper placement. It should be emphasized to the anesthesiologist that visual confirmation of the electrodes in contact with the vocal cords is essential. The electrode recording surface is often a blue strip or ring depending on the electrodes used. Common misplacements include electrodes that are too superficial or deep as well as a rotated tube [2].

Unlike EMG from spinal nerve myotomes, baseline EMG recorded from the vocal cords should not be quiet. At baseline, there should be some activity (25–50 μV) present in the recording. This is because the vocal cords are contracted at rest and relax when speaking. Failure to record baseline activity may be due to a number of factors including misplaced tube, use of lidocaine, or residual neuromuscular blockade. Asymmetric baseline activity may indicate that the ET tube and electrodes are rotated and not in contact with one side of the vocal cords. Inadequate baseline recordings will prevent proper monitoring during the case and could result in false-negative results. It is important to correct electrode placement if necessary. This is accomplished by asking the anesthesiologist to move the endotracheal tube while the monitorist views the live EMG recording. As the electrodes move into proper position, the amplitude of recorded activity on the screen will increase. The position showing maximal EMG activity should be marked and the tube secured. It is not unusual for baseline activity to decrease in amplitude during the procedure as a result of changes in electrode impedance resulting from increased secretions.

Identification of the RLN is one of the first steps in the thyroidectomy procedure. One technique, called sweeping, is used to aid the surgeon in initial dissection. Monopolar stimulation is used for the sweeping technique. The surgeon is given a handheld monopolar probe and the monitorist will stimulate continuously (at approximately 2 Hz) while the surgeon sweeps the field in search of the nerve. The presence of a CMAP response indicates that nerve is in proximity. There are technical considerations that the monitorist should be aware of during sweeping. The presence of blood or irrigation in the surgical field may shunt current away from the nerve and prevent a response from being seen despite proximity of the nerve to the stimulator [2]. It is therefore important that the surgical field remain dry when stimulating.

The stimulation parameters for sweeping are different than for direct nerve stimulation. The first difference is the use of a monopolar stimulator

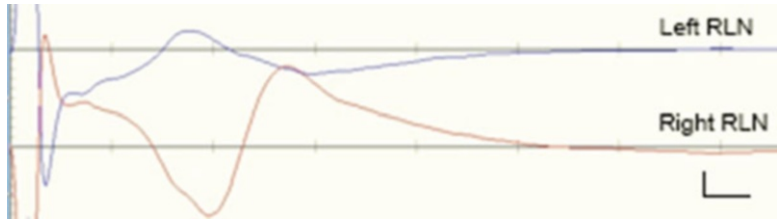

Fig. 16.3 Compound muscle action potential in response to stimulation of the RLN. CMAP recorded from the vocal cords bilaterally in response to stimulation of the right RLN. The stimulation intensity was supramaximal at 2.0 mA, causing the large resultant CMAP to be recorded in both channels. Scale bars indicate 1 ms and 100 μV

versus a bipolar stimulator used for direct nerve stimulation. Monopolar stimulation induces a larger current field and is said to be more sensitive than bipolar stimulation. Bipolar stimulation (having the cathode and anode in close proximity) has a smaller current field and while less sensitive is more specific. The stimulation intensity used for sweeping is higher than for direct nerve stimulation. Continuous stimulation up to 3 mA (pulse width not to exceed 50–100 μs) is performed until a response is seen. Once a response is recorded at supramaximal intensity, the intensity is reduced and the threshold for response determined. If there is no current shunting, the stimulation threshold can be used as an indicator of the distance to the nerve. The response should likewise increase in amplitude as the stimulator approaches the nerve.

When the surgeon is ready to confirm the identity of the RLN, direct nerve stimulation is the optimum method [13, 14]. Direct nerve stimulation uses a bipolar stimulator to find the threshold of activation by increasing the intensity of stimulation in 0.1 mA increments from 0 mA. The pulse width should not exceed 50–100 μs and the stimulation intensity should remain <2 mA. A CMAP recorded from the vocal cords with a latency of approximately 2 ms is confirmation of the identity of the RLN (Fig. 16.3). The stimulation threshold at this point can be used as a comparison to values at closing, possibly offering prognostic information to the surgeon on the function of the RLN.

It is common for the monitorist to not record a response to stimulation even when the surgeon expresses confidence that he is stimulating the RLN. There can be several reasons for this apparent discrepancy. The monitorist should immediately work to confirm that there are no technical issues preventing stimulation and recording. As mentioned earlier, the tube must be properly positioned to insure accurate recording, and this can be confirmed by recording of baseline spontaneous activity on both RLN channels. The presence of a stimulation artifact as well as measurement of current return will serve as confirmation of adequate stimulation. Once technical issues are ruled out, attention should turn to nature of the structure being stimulated. If the surgeon reports seeing a response visually within the field, then he is stimulating a motor nerve or a muscle directly. Often a visual response without EMG confirmation is due to stimulation of the SLN. If this is suspected, a pair of sterile needle electrodes can be handed off to the surgeon and placed in the cricothyroid muscle and an EMG response recorded. If there is no visual evidence of stimulation, then the surgeon may not be stimulating neural tissue or is possibly stimulating a sensory nerve, which will not produce an EMG response.

Continuous spontaneous electromyographic monitoring of the vocal cords is the modality by which injury to the RLN is avoided during the procedure. Spontaneous EMG is best viewed at a time scale of 200 μs/division and display sensitivity of 200 μV/division (Fig. 16.4). Occasional spiking or bursting indicates non-injurious proximity to the nerve while more clinically significant patterns of activity include training and neurotonic discharge. These latter two patterns should be immediately reported to the surgeon.

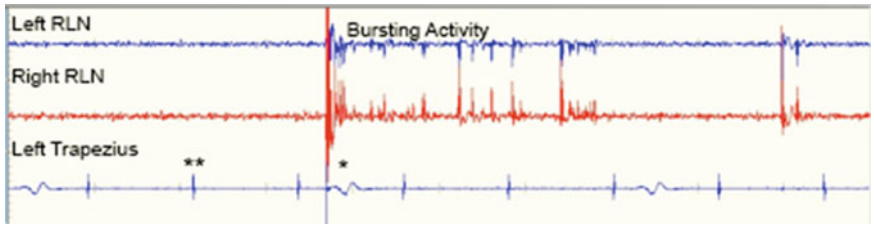

Fig. 16.4 Spontaneous EMG. Baseline EMG activity recorded from the vocal cords bilaterally and the trapezius (as a control). Note the tonic background activity of the RLN channels. Present in this record is bursting activity on the RLN channels. EKG (*asterisk*) and stimulation artifact (*double asterisk*) are seen in the trapezius recording

The use of audio EMG is useful in guiding the surgeon during the procedure. The surgeon may appreciate hearing spiking or bursting patterns as he navigates the surgical field. Spontaneous EMG is most useful in detecting impending nerve injury from stretch (retraction) or compression. Complete nerve transection may result in a quick burst of activity followed by electromyographic silence. Ischemic injury may go completely undetected by EMG monitoring.

Direct stimulation of the RLN at the conclusion of the procedure is recommended to document the function of the nerve. A similar method of thresholding the response employed as it was in the beginning of the procedure when the nerve was identified. Comparable thresholds can be taken as evidence of no new nerve damage during surgery [2].

In addition to intraoperative stimulation and monitoring of RLN function with spontaneous EMG, pre- and postoperative assessment of vocal cord mobility is useful for determining both preexisting pathology and postoperative outcome [2, 15]. The discovery of preoperative hemiparesis is important information that the surgeon and monitorist should consider before proceeding with the procedure. Careful intraoperative monitoring to avoid a bilateral injury is essential.

Parotidectomy

The parotid glands are the largest of the salivary glands, located on either side of the face just inferior and anterior of the ear (Fig. 16.5). Innervation of the parotid glands is by the glossopharyngeal nerve; however, the facial nerve travels directly through the parotid glands on the way to innervation of the muscles of facial expression. The parotids are a common site of tumor growth and as such may need to be surgically removed. The surgical plane artificially divides the parotid gland into a superficial and deep lobe. The facial nerve is the dividing line between the superficial and deep planes.

The facial nerve emerges from the brainstem between the pons and the medulla. The main function of the facial nerve is motor control of the muscles of facial expression. Extracranially, the facial nerve passes through the parotid gland where it divides into five major branches. This is why it can be said that parotid surgery *is* facial nerve surgery. A superficial parotidectomy will take out the portion of the gland superficial to the nerve plane. A deep lobe, or total, parotidectomy removes both superficial and deep lobes relative to the plane of the facial nerve.

During parotid surgery, facial nerve monitoring can assist the surgeon with functional preservation of the nerve [16]. IOM of the facial nerve for parotidectomy is largely similar to monitoring the RLN for thyroidectomy as presented above. Spontaneous and triggered EMG of the facial nerve can help to locate and identify the branches of the nerve, warn the surgeon of unexpected stimulation, reduce injury due to retraction and cautery, and evaluate nerve function at the conclusion of the surgery [15]. The five facial nerve branches that pass through the parotid gland are the temporal, zygomatic, buccal, marginal mandibular, and cervical. For a parotidectomy, needle electrodes are typically placed in

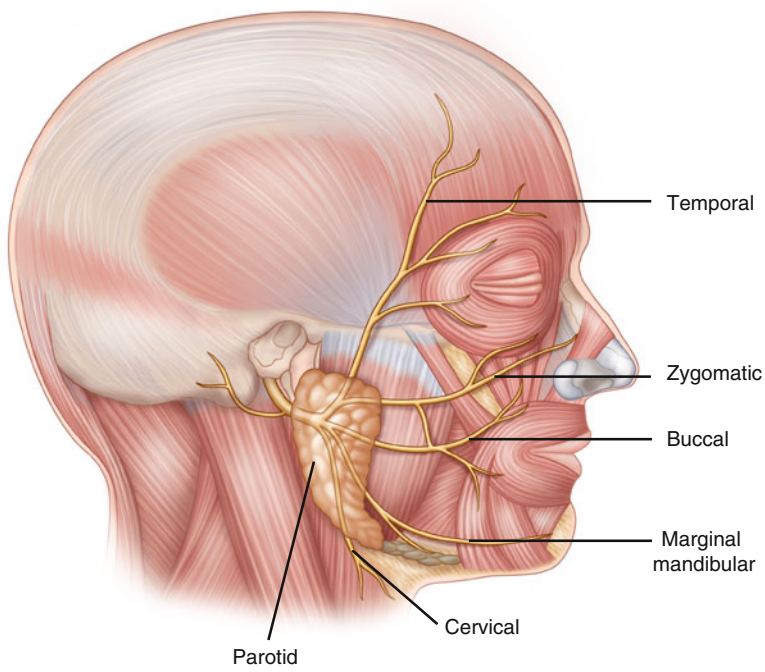

Fig. 16.5 Parotid gland and facial nerve

Table 16.1 Branches of the facial nerve and corresponding muscles for EMG

Branch	Muscles
Temporal	Frontalis
	Orbicularis oculi
Zygomatic	Orbicularis oculi
	Nasalis
	Zygomaticus major/minor
Buccal	Buccinator
	Orbicularis oris
Marginal mandibular	Depressor anguli oris
	Depressor labii inferioris
	Mentalis muscles
Cervical	Platysma

muscles corresponding to at least four out of the five branches (the cervical branch is often not monitored). Muscles commonly used are listed in Table 16.1. Recordings made from the frontalis or orbicularis oculi may be slightly noisier than other channels due to contamination by frontal EEG signals. Stimulation of the facial nerve during surgery assists the surgeon in identifying the facial nerve and distinguishing neural from nonneural tissue. Like RLN monitoring, direct nerve stimulation is the only way to reliably identify the nerve [17]. Typical parameters used are a stimulation intensity of 0.1–2.0 mA with a duration of 50–100 μs [17]. The latency of the facial nerve response when stimulated at the brainstem is approximately 7 ms, but a response when stimulated at the parotid will be shorter, so time base should be adjusted accordingly. The stimulation threshold for the facial nerve should be recorded and compared with stimulation of the nerve following parotidectomy. At closing, functional integrity of the facial nerve can be assessed by stimulating each branch of the facial nerve. Closing stimulation thresholds of <0.5 mA are prognostic for normal postoperative function of the facial nerve [15, 17].

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Peripheral Nerve Monitoring

17

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Introduction

The peripheral nervous system is comprised of a complex and vast network of nerves that work synergistically to achieve unique functions in the human body. Neuronal diversity lends nerves in this system to be vulnerable to a variety of injury types that have different management strategies. Peripheral nerve monitoring has been proven to be a useful asset for intraoperative management of nerve lesions. Physical examination alone of nerve lesions has been shown to be an unreliable and often misleading method to assess nerve integrity and regeneration. Intraoperative peripheral nerve assessment provides clinicians with unique, real-time information that is otherwise unavailable via preoperative nerve examination. This additional information can help to guide clinical decision making and subsequently improve patient outcomes. This chapter will provide a brief overview of the physiology and anatomy of the peripheral nervous system, review nerve injury classifications, and detail the equipment and techniques utilized for effective intraoperative peripheral nerve assessment.

Overview of Peripheral Nervous System

Before understanding the pathophysiology of specific lesions in the peripheral nervous system (PNS), it is imperative to have basic knowledge of both the anatomy and physiology of the PNS. The PNS serves many purposes in the human

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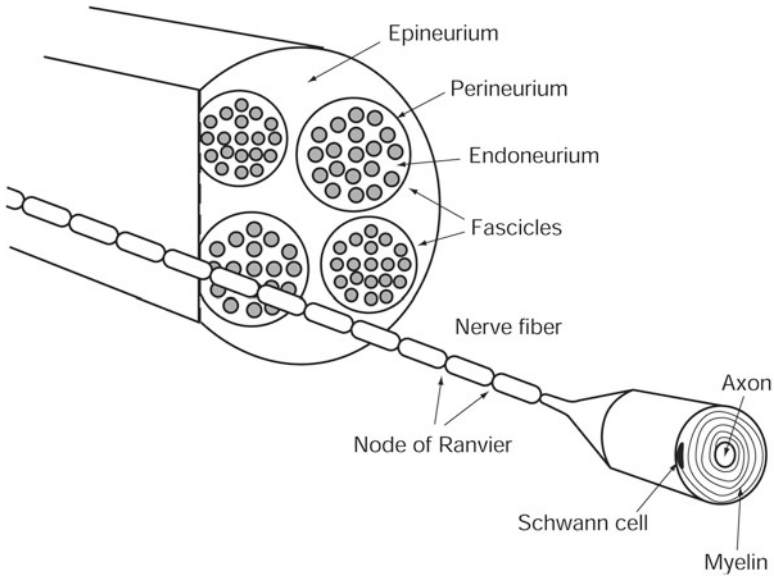

Fig. 17.1 Anatomical organization of a peripheral nerve. With kind permission from Springer Science+Business Media: Sunderland S. A classification of peripheral nerve injuries producing loss of function. Brain. 1951;74:491–516

Table 17.1 Conduction velocity in nerve fibers of different types

Fiber type	Function	Average axon diameter (mm)	Average conduction velocity (m/s)
Aα	Motor nerves, primary Muscle-spindle afferents	15	100 (70–120)
Aβ	Mechanoreceptor afferents	8	50 (30–70)
Aδ	Temperature and pain afferents	<3	15 (12–30)
C	Pain afferents Sympathetic postganglionic fibers	~1	1 (0.5–2)

body including regulating motor, sensory, proprioceptive, and pain functions. The majority of peripheral nerves are myelinated; however, there is a subset of nerves that are unmyelinated. While myelin in the central nervous system is made from oligodendrocytes, myelin found in the peripheral nervous system is synthesized from Schwann cells [1]. The transition zone between the peripheral nervous system and central nervous system is called the Obersteiner–Redlich zone and is an area most vulnerable to injury [1]. Peripheral nerves contain many axons. Individual axons are separated from each other by a thin connective tissue sheath called the endoneurium. Groups of endoneurium-lined axons form fascicles that are surrounded by a connective tissue layer called perineurium. Groups of fascicles subsequently form nerve trunks, which are covered by the outermost layer called epineurium [2]. Figure 17.1 illustrates the organization of a peripheral nerve. The endoneurium, or central portion of the nerve, is composed of finer collagen fibrils when compared to the peripheral portions of the nerve. This in turn results in the central portion of nerves being more sensitive and fragile to traction [1].

Nerve fibers in the peripheral nervous system consist of the myelinated Aα, Aβ, and Aδ fibers and the unmyelinated C fibers (Table 17.1). These nerves are further classified based on axonal diameter, which also dictates nerve conduction velocity [1]. Motor nerves are made of Aα fibers, have the biggest diameter, and have the fastest conduction velocity at about 100 m/s [1].

Motor neuron cell bodies are located in lamina IX of the ventral horn of the spinal cord [3]. Sensory nerve fibers consist of the myelinated Aβ and Aδ and unmyelinated C fibers. These nerve fibers have cell bodies located in the dorsal root ganglia of the spinal cord [4]. Aβ fibers are mostly responsible for low-threshold cutaneous receptors and have an average conduction velocity of 50 m/s [5]. Nerves that are responsible for pain transmission consist primarily of the unmyelinated C fibers. These have the slowest conduction velocity [5].

Peripheral Nerve Injuries

Peripheral nerve injuries can result from a variety of mechanisms. A recent retrospective review of 1,019 operative brachial plexus lesions showed that the majority of lesions resulted from stretch or contusion and were in continuity. A smaller proportion resulted from tumors, gunshot wounds, and transection due to sharp laceration [6]. The management of injuries from sharp laceration and blunt transection is relatively straightforward consisting of primary repair within 72 h and 2–3 weeks, respectively [7, 8]. However, lesions found in continuity pose several confounding variables that require extensive preoperative evaluation and planning [6, 7, 9]. Intraoperative neurophysiological assessment of peripheral nerve lesions is useful in determining continuity and establishing a treatment plan.

Classifications of Injuries

Focal peripheral nerve injuries can be classified into three main categories based on the morphological and functional features of the lesions: neurapraxia, axonotmesis, and neurotmesis. Lesions can also be divided into five groups known as Sunderland grades (Fig. 17.2).

Neurapraxia is the mildest form of injury. It is defined as partial or complete conduction failure without any structural changes in the support structures of the nerve [10]. This type of injury can also be classified as Sunderland grade 1. Etiology of this type of lesion can be due to excessive stretch, heat, or compression. The affected nerve is able to regain full function within several hours to days [1].

Axonotmesis is defined as the interruption of nerve axons without damage to its supporting connective tissue or glial structures. This is a more significant injury and can also be identified as Sunderland grade 2 [11]. Injuries such as this can also result from excessive stretch, compression, or pinching [1]. Lesions that occur distally to the cell body result in Wallerian degeneration of axonal components distal to the lesion. Wallerian degeneration is defined as the degenerative changes that occur in a segment of a nerve fiber when continuity with its cell body is lost [1]. Wallerian degeneration begins immediately after the lesion has occurred and is usually complete within 48–72 h after the injury. It is important to note that the nerve may still be able to conduct impulses within the first 24–72 h after the injury [1, 11]. Intraoperative assessment in this immediate time frame, therefore, may be inaccurate.

Neurotmesis is defined as injury that involves both the axons and neural support structures such as Schwann cells and connective tissue layers. This is the most severe type of injury and can be further classified as Sunderland grades 3, 4, and 5 [10]. Sunderland grade 3 injury involves a mixture of support structure and axon damage. This degree of injury may be able to undergo partial regeneration without intervention and subsequently regain some level of function. Sunderland grade 4 injuries result in scar formation over the entire cross section of the nerve [12]. The differentiation between grade 3 and 4 lesions is essential because spontaneous regeneration may be blocked by scar tissue in grade 4 injuries. Thus for grade 4 lesions, surgical intervention is indicated to remove the offensive scar tissue and allow for optimal recovery [12]. Sunderland grade 5 injuries are the most severe form of injury and are described as total transection of a nerve. This degree of injury requires immediate surgical grafting in an attempt to restore any functionality. Nerve grafting involves surgical removal of the injured segment of the nerve and connecting the two functional ends with a graft taken from an

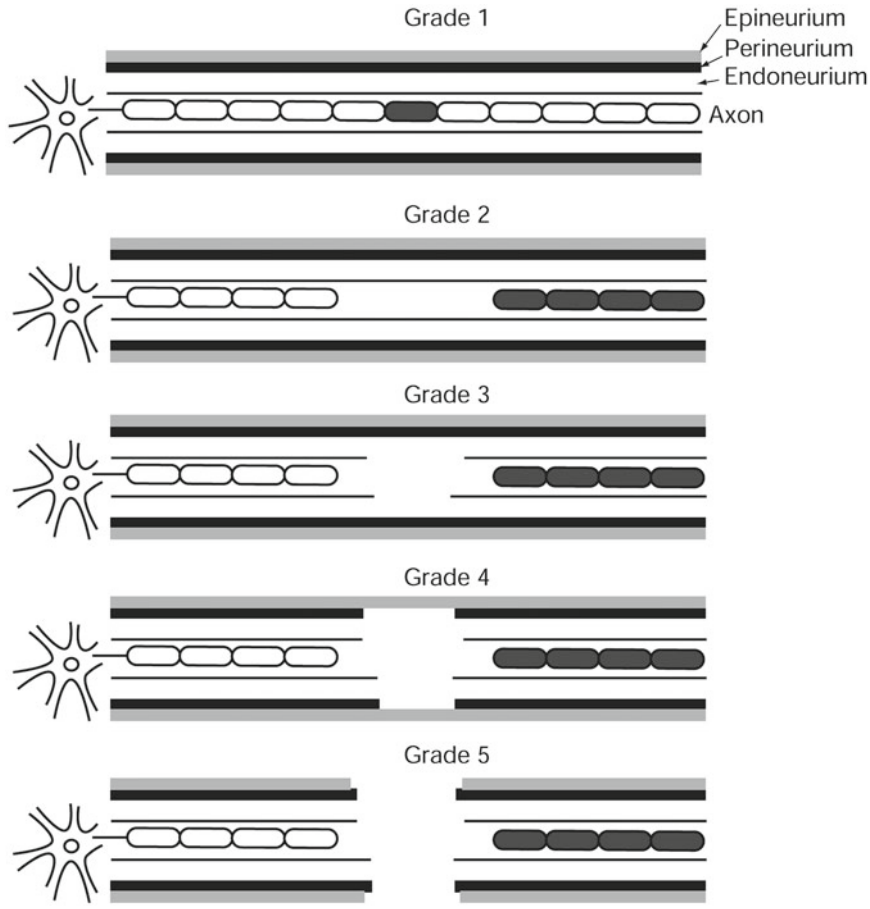

Fig. 17.2 Illustration representing Sunderland grading and showing the various degrees of conduction block and support structure changes inherent to each grade of injury. With kind permission from Springer Science+Business Media: After Sunderland S. Cranial nerve injury. Structural and pathophysiological considerations and a classification of nerve injury. In: Samii M, Jannetta PJ, editors. The cranial nerves. Heidelberg: Springer; 1981. p. 16–26

autologous site. Usually the sural nerve is used to provide graft tissue (Fig. 17.3).

When considering the degree of neuronal injury, it is important to also understand the basic physiology of neuronal regeneration. Nerve regeneration is a complex process that is very different in humans compared to lower mammals, which have much greater regenerative capabilities [13–15]. As mentioned earlier, axonal components distal to the lesion undergo Wallerian degeneration, while the proximal part seals off at the point of division [12]. The proximal sealed portion will produce multiple sprouts of growing neurites within approximately 36 h of the injury. Regeneration occurs at a speed of approximately 1 mm/day [1]. This increase in growth can actually result in a greater concentration of axons distal to the lesion compared to proximal axon counts [12]. However, these growing axons have a much smaller diameter with distinct electrical properties [16–18]. They have much slower conduction velocities relative to normal nerves [12]. They also have significantly higher electrical thresholds relative to normal nerves. Effective regeneration is characterized by some fibers increasing in diameter, while other finer fibers regress and die. Axons must reach a critical diameter in order to produce a useful motor unit.

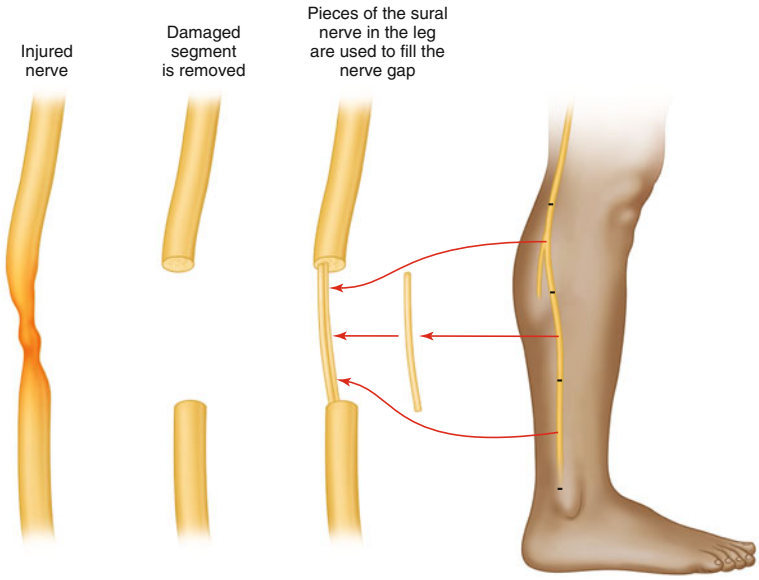

Fig. 17.3 An example of using the sural nerve to graft two segments of an injured peripheral nerve

If the developing small-caliber fibers do not successfully increase in diameter, there is low probability that they will be able to form a meaningful connection with the corresponding muscle [12, 13, 15]. Thus the presence of numerous fine fibers may be indicative of either active early-stage regeneration or later-stage failed regeneration.

Preoperative Evaluation of a Peripheral Nerve Injury

Crum et al. detail four critical questions that should be addressed when evaluating all peripheral nerve injuries [19]. First, it is obviously vital to identify whether the problem is truly neurologic. Poor patient effort, pain, and the subjective nature of sensory examinations can decrease the accuracy of clinical evaluations. Next, it is important to localize the specific nerve that is affected. This is largely dependent on clinician knowledge of peripheral nerve anatomy and dermatome distribution [19]. The clinician must then try to identify where the lesion is located along the anatomical course of the nerve. Lastly, it must be determined whether the lesion is complete or not. As discussed previously, it is possible that lesions in continuity may be undergoing axonal regrowth that is not yet detectable via clinical examination alone. Prior to the advent of electrophysiological testing, surgeons had to rely on visual inspection to determine a course of treatment. Today, real-time electrophysiological recordings can provide an accurate diagnosis of the lesion allowing the surgeon to formulate a well-informed treatment plan. Generally, lesions found to be in continuity are observed for subsequent regeneration, while lesions in which there is no continuity are grafted [6, 20].

Recording Nerve Action Potentials

Peripheral nerve lesions that result in axonal sprouting can form an accumulation of misdirected neurites known as a neuroma. Neuromas can be small or large and cause compression of the nerve resulting in even more injury. Frequently, functionally regenerating axons may pass through the neuroma on their way to reestablish connections with their targets. These are known as neuromas in continuity. Such neuromas in continuity may need to undergo neurolysis so the regenerative process may continue, but do not

require grafting. Neurolysis is the surgical freeing of the nerve from inflammatory adhesions and resulting traumatic neuroma. The concept of diagnosing a neuroma in continuity is a simple one; stimulate a peripheral nerve proximal to a lesion and use electrodes to monitor for a response distal to the lesion. Intraoperative monitoring can be accomplished using relatively simple and inexpensive equipment. The majority of commercially available EMG machines are able to effectively detect compound nerve action potentials (CNAPs). It has been estimated that a minimum of 4,000 fibers are needed to produce a clear CNAP [21].

Since the size of most CNAPs is considerably larger than the typical evoked potentials recorded in operative monitoring, the process of signal averaging is not required [21]. The amount of stimulation required is dependent on the size of the nerve being studied. It is recommended that the stimulator be able to produce short pulses of 0.02–0.05 ms and intensities of up to 70 V [12]. The use of short-duration pulses helps to identify the type of fibers being stimulated. Fine fibers of regenerating axons and other small-diameter fibers are much less sensitive to short-duration impulses compared to healthy nerves [21]. Stimulation of nerves in short duration through electrodes in direct contact has been proven to be both safe and effective [21]. Longer-duration stimulation may result in electrical burns or other iatrogenic injury [21].

Electrodes used to stimulate and record CNAPs are also simple. They should fulfill certain characteristics, such as being durable, functional, and reliable, and have electrical properties conducive for use in electrical stimulation [12]. It is imperative that the electrodes never be made from silver due to the potential damage from deposited silver salts [12]. Stainless steel has proven to be a cheap, effective, and readily available option for electrode composition. Electrode size can be modified to better accommodate the size of the nerve being studied. Electrode tips can be bent into a "J" or hook shape in order to better grasp and isolate the desired nerve (Fig. 17.4). The stimulating electrode is usually tripolar, whereas the recording electrode is bipolar [21]. The tripolar configuration for stimulation helps to reduce stimulus artifact and limit spread of the stimulus. The amplitude of CNAPs recorded is dictated by the distance between recording electrodes [12]. The ideal distance between recording electrodes is anywhere from 3 to 7 mm depending on the size of the nerve. If the electrodes are too close together, the recorded action potential can have falsely reduced amplitude. Reasoning behind this phenomenon is due to the characteristic saltatory conduction seen in myelinated nerves, being necessary for the recording electrodes to span at least one node of Ranvier [12, 16, 17].

Once the desired nerve is properly isolated, the electrodes are used to study CNAPs from both the proximal and distal segments of the nerve. If no CNAP can be recorded distal to the lesion in response to proximal stimulation, there is little chance that the nerve will be able to undergo primary regeneration. The ability to record a distal CNAP indicates that the lesion is in continuity. Precise determination of the location of the lesion may be accomplished using a technique known as "inching" or "walking" of the electrodes. This technique entails stimulating the nerve at short, incremental steps across a lesion and assessing the change in morphology and latency of the waveforms that are recorded distally [19, 22].

Technical Considerations

There are several technical aspects that need to be considered when evaluating a peripheral nerve injury. First, adequate exposure and isolation of the nerve being investigated is essential. This helps to ensure that the responses being recorded are truly representative of only the nerve being investigated [6]. Adequate isolation also ensures the electrodes are in good contact with the nerve [6]. The nerve should be free of both excess irrigation and blood to reduce the prevalence of stimulus artifact and shunting of current. The hook configuration of the electrodes may be used to slightly elevate the nerve out of any fluid. The

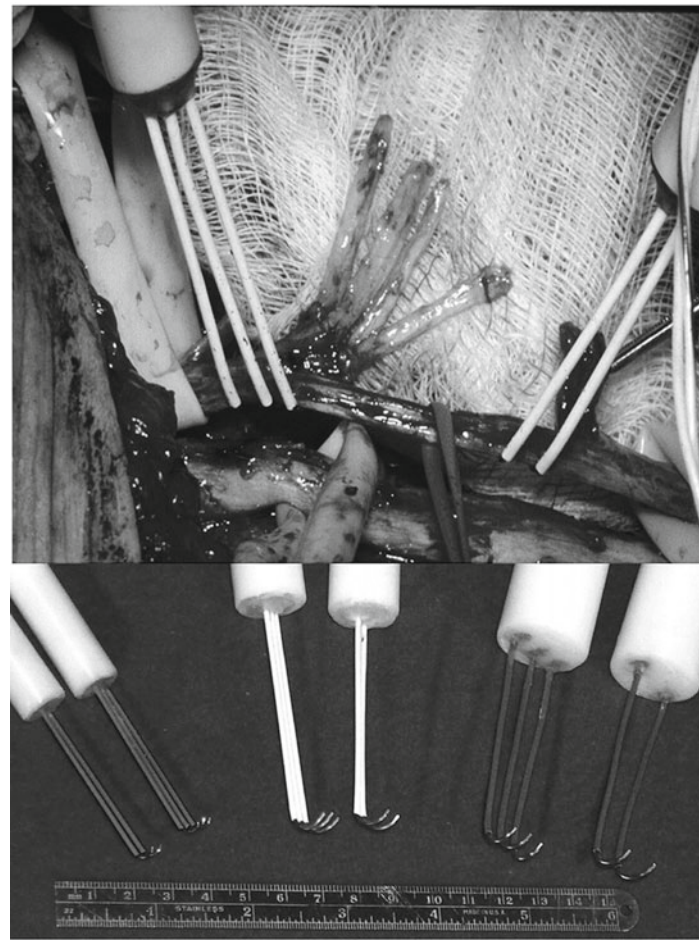

Fig. 17.4 *Top panel* shows tripolar stimulation and bipolar recording from a peripheral nerve intraoperatively. The electrodes span a few centimeters of the nerve. The *bottom panel* shows a selection of hook electrodes that may be used to stimulate and record from peripheral nerves. With kind permission from Springer Science+Business Media: "Surgery in the peripheral nervous system," Monitoring of the nervous system for anesthesiologists and other health care professionals, Happel, Fig. 35.1

exposed nerve will inevitably lose heat in the cold operating room environment. Healthy, cold nerves will have poor conduction velocity compared to normothermic healthy nerves [6]. Investigators recommend using warm saline prior to stimulation to prevent temperature distortion. If a tourniquet has been used, approximately 20 min should pass before nerve recordings take place. The use of excessive local anesthetic may also attenuate or block nerve conduction [6]. The temporal relationship between the intraoperative investigation and time of injury is just as important as the procedural aspects of investigation [23, 24]. As mentioned previously, no studies should be done on lesions in continuity within 72 h of the injury because that is still within the time frame of Wallerian degeneration. Lastly, care must be taken to ensure the distance between electrodes is adequate for correct interpretation of the signal. Recording a NAP over a known normal portion of nerve can be useful to serve as a control (Fig. 17.5). This can be beneficial if there is any question about the validity of an absent NAP over a lesion [19].

Anesthesia has little effect on either NAP or CNAP recordings. Neuromuscular blockade may be desirable to reduce excessive muscle artifact for NAP recordings [19]. Neuromuscular blockade should be avoided if muscle recordings will be performed with peripheral nerve stimulation. Inhalational anesthesia has no known affects on peripheral nerve monitoring.

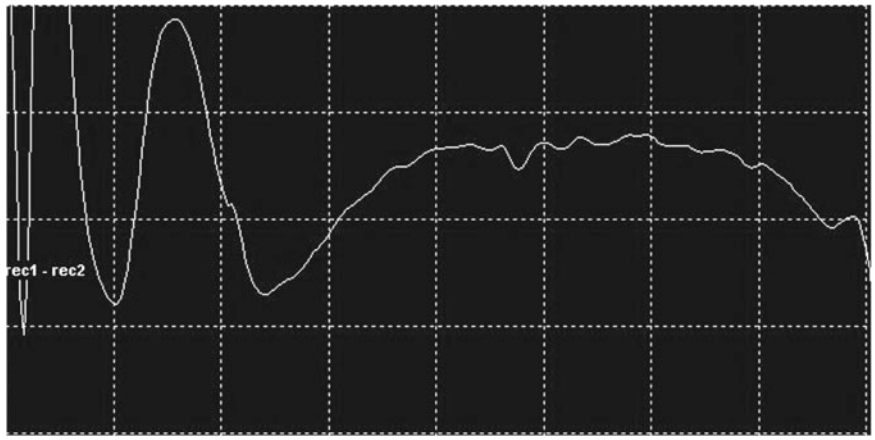

Fig. 17.5 A CNAP in response to stimulating and recording from a segment of peripheral nerve proximal to a tumor. The fact that the CNAP is normal in appearance is because it is recorded proximal to the tumor. The early latency suggests that there is a short distance between the stimulating and recording electrodes. With kind permission from Springer Science+Business Media: "Surgery in the peripheral nervous system," Monitoring of the nervous system for anesthesiologists and other health care professionals, Happel, Fig. 35.4

Intraoperative Diagnosis and Treatment of Peripheral Nerve Injury

There are several characteristic findings of NAPs from injured nerves. First, an increase in latency can indicate impaired conduction velocity [25]. Latency is determined as the time between the onset of the stimulus and the earliest negative peak of the response [25]. A decrease in the amplitude of the negative peak in response to maximal stimulation can also be representative of fewer fibers being recruited (Fig. 17.6) [25].

Except in certain circumstances, lesions in continuity are generally treated by neurolysis, and then regeneration is allowed to proceed [19, 26]. Grafting of a nerve in continuity is only indicated in lesions with no documented CNAP and thus little or no chance for effective regeneration [9, 19]. Most nerves with a lesion in continuity are allowed to regenerate following neurolysis and do not require grafting. The treatment of a complete nerve transection is surgical intervention (grafting) within days to weeks of the initial insult [7, 8]. Figure 17.7 shows a flow chart that is useful in determining the course of treatment based on electrophysiological observations.

Specific Nerve Lesions

Carpal Tunnel Syndrome

Median neuropathy at the wrist is the most common entrapment neuropathy of the upper extremity [9]. Intraoperative nerve monitoring is seldom used in this scenario due to the effectiveness of preoperative evaluation and ease of the decompressive procedure. However, intraoperative studies have shown sites with the most abnormal NAPs correlated with the segment of most abnormal-appearing nerves [27]. The anatomical site noted to have the most abnormal conduction is within the first 10–20 mm distal to the proximal border of the flexor retinaculum. Conduction has been documented to either improve or stay the same immediately after median nerve decompression [28, 29].

Ulnar Neuropathy

Ulnar neuropathy at the elbow is the second most common entrapment neuropathy. The two most common anatomical sites for compression at the elbow are at either the cubital tunnel or

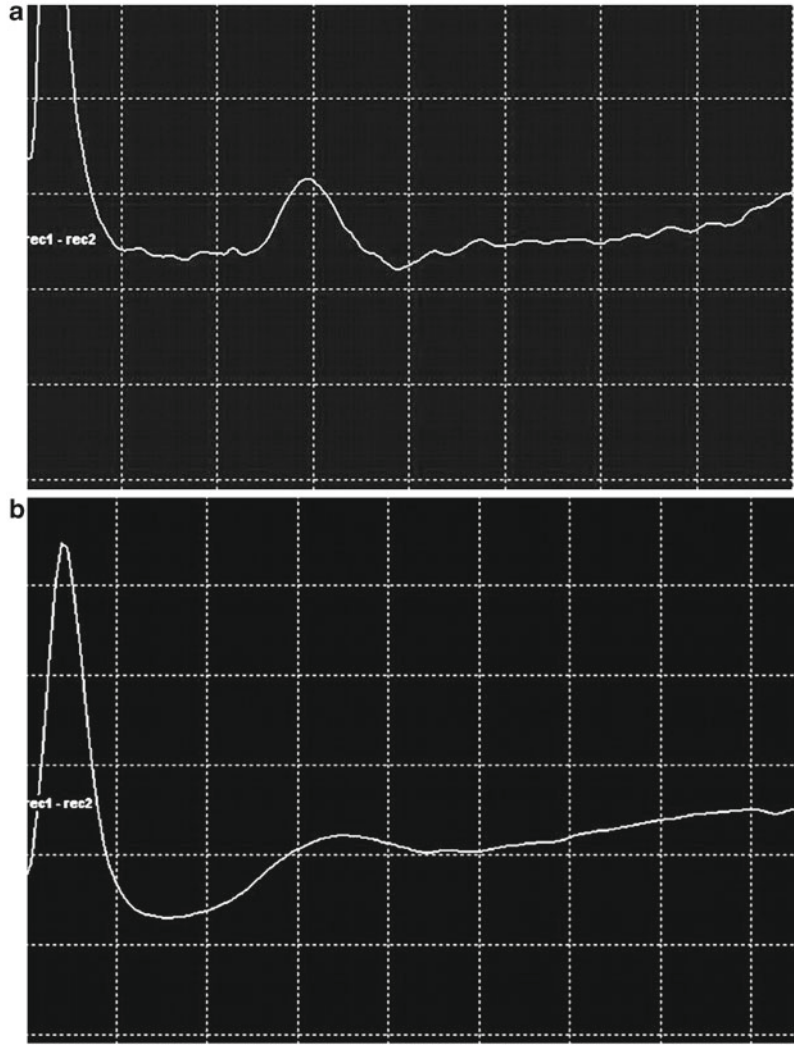

Fig. 17.6 (**a**) CNAP recorded from a nerve of the brachial plexus. Note the normal appearance of morphology and duration (scale: 200 μV/div, 1 ms/div). (**b**) Abnormal CNAP recorded from a nerve of the brachial plexus. Note the increased duration (area under the curve) and lower amplitude. Physiologically this suggests both changes in conduction velocities among the individual nerve fibers and recruitment of fewer fibers (scale: 200 μV/div, 1 ms/div). With kind permission from Springer Science+Business Media: "Surgery in the peripheral nervous system," Monitoring of the nervous system for anesthesiologists and other health care professionals, Happel, Fig. 35.2

retroepicondylar groove between the medial epicondyle and olecranon [9]. Preoperative nerve studies are able to confirm the presence of neuropathy but may not be able to localize the lesion between these two sites [30, 31]. This is important because the surgical approach for treatment is different for the two sites. Numerous studies have shown that the site most frequently implicated is at the level of the epicondyle [32]. This is a prime example where intraoperative monitoring can guide clinical management and improve patient outcomes.

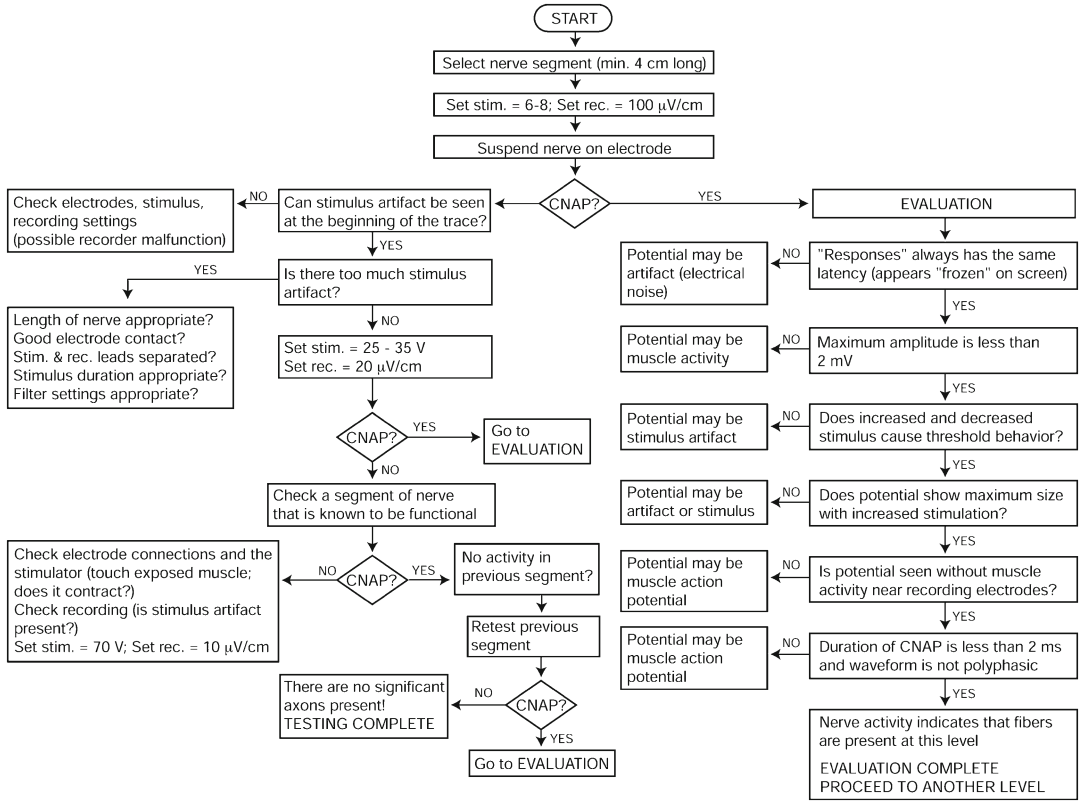

Fig. 17.7 Flow chart of clinical decision making for intraoperative peripheral nerve diagnosis. With kind permission from Springer Science+Business Media: Intraoperative neurophysiological monitoring, 3rd edition, 2011, Moller AR, Fig. 15.3

Common Peroneal Neuropathy

The common peroneal nerve is most commonly affected as it traverses the fibular head at the knee [9]. While identification of neuropathy can be identified preoperatively, intraoperative nerve studies can assist with localization and determination of nerve continuity [27]. A large series of surgically repaired peroneal neuropathies revealed that lesions with no NAP were much more likely to be due to trauma. These types of lesions were grafted. Lesions with recordable NAPs were most likely related to nontraumatic compression or entrapment. These lesions appropriately underwent neurolysis as opposed to grafting [33].

Conclusion

The vast majority of peripheral nerve injuries leave the nerve in some degree of continuity. Lesions in continuity may create a spectrum of damage within the nerve often precluding an accurate diagnosis with conventional preoperative EMG evaluation [21]. Intraoperative peripheral nerve monitoring synergistically combines several basic concepts that can help provide definitive and real-time information on the status of the fiber population within the nerve. Successful implementation is multifaceted and requires effective communication amongst the surgeon, neurophysiologist, and anesthesiologist.

When used effectively, intraoperative peripheral nerve monitoring has been proven to improve both treatment efficacy and patient clinical outcomes.

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Intraoperative Cortical Mapping: Basic Concepts, Indications, and Anesthesia Considerations

18

Art Saus, Charles Fox, Harish Bangalore Siddaiah, Alan David Kaye, Scott Francis Davis, and Bharat Guthikonda

Introduction

The eloquent area of the brain is responsible for written and verbal communication. Functional neuroimaging indicates that interindividual variation exists with the anatomical location of the eloquent area of the brain. Some patients have shown significant contribution from areas located near, but outside of, the traditionally recognized eloquent area. Classically, these areas adjacent to or near the eloquent area were thought to have little impact on written or oral language skills, and many neurosurgeons, in the past, underestimated the impact of operating in these areas. Now, each patient is known to have a unique eloquent area. This necessitates intraoperative cortical mapping to more accurately identify functioning before removing brain tissues in patients undergoing epilepsy or brain tumor surgery in areas near this region of the brain. The goal of intraoperative cortical mapping is to maximize surgical resection in the eloquent area while minimizing the incidence of permanent disabilities. This chapter is intended to provide you with the concepts, indications, and anesthetic considerations important to intraoperative cortical mapping and to prepare you for further reading of more advanced texts and primary literature on this topic.

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Concepts

Cortical Mapping: Historical Perspective

Dr. Robert Bartholow performed the first electrical stimulation of the cortex in 1874 on a patient named Mary Rafferty, a 30-year-old Irish woman who had been employed as a domestic servant. She presented with an infected scalp ulcer, which was diagnosed as cancerous. The physicians attempted to treat this surgically, leaving a 2-in. diameter hole in her skull with exposed dura. Apparently after determining that nothing could be done to save her life, Dr. Bartholow proceeded

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to experiment on the exposed brain, reportedly with the patient's consent. By inserting needle electrodes into the exposed brain tissue and by applying small electrical currents to various areas, he noticed it caused movements in various parts of her body, and did not cause pain, following the patient's initial complaints of neck pain with needle insertion. He also noted that application of larger currents resulted in seizure activity and what seems to be what we now recognize as a transient post-ictal state. Although it is reported that she returned to consciousness 20 min later, she complained of weakness and vertigo. As her condition worsened, her physicians did not do any further experiments, and she died a few days later. The conclusions from her autopsy were that although parts of her brain had been damaged from the electrodes, her death was due to her cancer and not to this experiment. Despite this "contribution to medical science," both British and American physicians severely criticized Dr. Bartholow and his "reckless use of living human beings," and the American Medical Association condemned his experiments, calling them "so in conflict with the spirit of our profession, and opposed to our feelings of humanity that we cannot allow' them to pass unnoticed" [1].

Despite this criticism, and the fact that this hardly could be considered "cortical mapping" in any sense of our current use of the term, this provided to beginnings of understanding that electricity could be applied to different areas of the brain and that regional somatic activity would result. Research on electrical stimulation of human and animal brains continued, and in 1888 Dr. Nancrede mapped the motor cortex by the use of a battery-operated bipolar stimulator probe. Neurologists David Ferrier and Victor Horsley used cortical stimulation mapping techniques to research the function of the precentral gyrus and the postcentral gyrus in the late 1800s. In the early 1900s Charles Sherrington used monopolar stimulation to elicit responses and was able to determine that the precentral gyrus elicited a motor response and that the postcentral gyrus was a sensory cortex. Dr. Harvey Cushing confirmed these findings and was the individual primarily responsible for moving cortical mapping from an experiment into an accepted neurosurgical technique.

Prior to going into the techniques used in the process of cortical mapping and analysis of those determinations, we should first have some understanding of what a cortical map is. Most physicians and medical students have seen the diagram of the homunculus, as described in the 1930s by a Canadian neurosurgeon, Dr. Wilder Penfield, and probably remember an image of a human body displayed across a drawing of a human cortex, although in a somewhat disjointed manner, with a large elongated face in the lateral one-third, while the hand is in the next approximately one-third, and the rest of the body is in the next one-third, toward the most central part, then with the foot on the medial portion of each hemisphere (see Chap. 2). Most physicians will probably also remember that the sensory functions are shown as existing in the postcentral gyrus of the parietal lobe, just posterior to the central (or Rolandic) sulcus, while the motor function in the cortex is described as primarily in the precentral gyrus of the anterior lobe, just anterior to the central (Rolandic) sulcus (with a very similar homunculus image). In effect, this displays the most basic concept of a cortical map. Unfortunately, however, this homunculus diagram is a grossly inaccurate oversimplification. The anatomical view of the brain tissue does not always precisely correlate to localizing the functions as suggested by this diagram. Sensory and motor areas of the cortex can now be mapped much more precisely by electrical stimulation and recording of "evoked" responses.

Anatomic and Physiologic Basis

The cortex of the human brain is 2–4 mm thick and in most parts of the cerebrum contains six layers which can rather easily be demonstrated on microscopic examination. In general, sensory cortex is thinner and motor cortex is thicker [2]. Within the brain cortex, very small areas (minicolumns) can be identified that perform a specific information processing function. Minicolumns grow from progenitor cells within the embryo

and contain neurons within multiple layers (2–6) of the cortex [3]. A cortical minicolumn is a vertical column through the cortical layers of the brain, comprising approximately 80–120 neurons, except in the primate primary visual cortex, where there are typically more than double this number. There are about 200,000,000 minicolumns in the human cortex. Many sources support the existence of minicolumns, especially Mountcastle [4] with strong evidence reviewed by Buxhoeveden and Casanova [5] who conclude "… the minicolumn must be considered a strong model for cortical organization" and that the minicolumn is "the most basic and consistent template by which the neocortex organizes its neurones, pathways, and intrinsic circuits." It appears that this minicolumn structure is the primary means of organization in the cerebral cortex not only of humans but of other animals as well.

From multiple examinations and calculations, various researchers have estimated the diameter of a human minicolumn is about 28–60 μm. These minicolumns also contain downward projecting axons that are approximately 10 μm in diameter, with periodicity and density similar to those within the cortex, but not necessarily coincident. The probable estimated size of a minicolumn can also be calculated by area considerations: if the surface area of a human cortex (both hemispheres) is 1.27×10^{11} μm^2 and if there are 2×10^8 minicolumns in the cortex, then the cortical surface area of each minicolumn is 635 μm^2, giving an average diameter of 28 μm (but even if the cortex area were doubled to the commonly quoted value of 2.5×10^{11} μm^2, this would rise to 40 μm). Johansson and Lansner do a similar calculation and arrive at an estimated minicolumn size of 36 μm.

There is also evidence from studies published in 2000 by two separate researchers, Buxhoeveden and Buldyrev, that spacing of 50–80 μm exists between adjacent columns. All cells in a single minicolumn have the same receptive field; adjacent minicolumns may have very different fields. Thus, a stimulus applied to a specific sensory nerve elicits a response within specific cortical minicolumns and does not necessarily elicit responses in immediately adjacent minicolumns in the cortex. This columnar arrangement forms the anatomic basis for the ability to perform cortical mapping. However, electrodes which are used for cortical mapping currently have a diameter of 2–3 mm, so we cannot electrically stimulate each discrete minicolumn but instead electrically stimulate a field containing hundreds of minicolumns with (hopefully) common functionality.

Maps of these cortical areas may be demonstrated in different ways such as texture maps, color maps, and contour maps. However, despite the existence of these maps, even for those attempting to localize the fields of "minicolumns" which subserve a particular function in a human brain, it can be challenging. The brain retains a great degree of plasticity, such that if one of these areas is damaged, much of the function designated to that specific area can be "taken up" or assumed by a nearby area. Thus, designated maps can change with experience.

As an example of this plasticity phenomenon, people who read Braille (which is done with an index finger) develop large areas responsive to stimulation from the index finger. A homunculus mapped on the motor cortex of such a person would have a relatively huge index finger. This phenomenon contributes to the lack of accuracy and specificity of a "brain map" that the standard homunculus diagram would otherwise suggest is present in the human brain.

The cytoarchitecture of the cerebral cortex enables the recording of local positive and negative potentials over the cortical surface corresponding to the projection of cortical axons. As discussed in Chap. 4, this phenomenon is known as a dipole. The projection of dipoles varies among locations of the cortex, but the projection of the dipole of neurons in the primary somatosensory cortex (postcentral gyrus) is in the anterior–posterior plane. Furthermore the zero-potential or mid-dipole point lies over the central sulcus. As such, recording the cortical peak of the median nerve SSEP from a row of electrodes placed directly on the cortical surface is used as a means of locating the central sulcus and therefore both the primary motor and sensory cortical areas. The point at which a phase reversal

(between positive and negative potentials) is seen can be reliably marked as the central sulcus. See Fig. 4.3 in Chap. 4 for an example. Once the relative location of the motor cortex is identified, it can be further mapped as described below.

Equipment and Technique

So how is cortical mapping accomplished? The mapping is done during a craniotomy by stimulating the sensory or motor cortex with a weak electric current, usually for a few seconds, once the dura mater has been peeled back. This electrical stimulation acts as a transient reversible virtual lesion, interrupting the normal electrical activity in that localized area of neural tissue. This "lesion" can either induce or prevent a specific motor or sensory response that can be tested and evaluated. For example, the stimulation may produce tingling in part of the body, or movement in part of the body, or it can interfere with a normally spoken word.

As mentioned earlier, the electrodes currently used are usually circular with diameters of 2–3 mm. They are usually made of stainless steel or a platinum/iridium alloy and imbedded in a Silastic material. Due to difficulty in re-sterilizing them, they are single-use devices.

Stimulation for mapping is commonly performed according to one of two techniques. Using continual electrical stimulation (Penfield's method), constant current is applied using a bipolar stimulating electrode at a frequency of 50–60 Hz. A biphasic square wave pulse with duration of 400–1,000 μs is used in order to avoid charge buildup on the surface of the brain. A monophasic square wave pulse is not safe to use for this type of high-frequency continuous stimulation. A more modern stimulation technique used for mapping of the somatic motor areas is known as direct cortical electrical stimulation (DCES) or simply MEP mapping because of the similarity with transcranial motor evoked potential monitoring. DCES makes use of a pulse train as opposed to continuous stimulation. Monopolar anodal stimulation is used for DCES and due to the use of brief pulses; monophasic square waves are an acceptable stimulus. A train of 4–9 pulses with duration of 50–500 μs is usually effective. Electrodes may be placed individually or more usually in a row or in a grid array. The electrical current applied must be enough to stimulate the neurons for an adequate duration yet low enough to avoid damaging them. Whether using MEP mapping or Penfield's technique, the "dose" of the current is usually started low and then gradually increased in both intensity and duration until a response is elicited. So initial intensities of 1 mA are a commonly used starting point. The current is then gradually increased by 0.5–1 mA with successive tests until a desired response is noted. It is important to identify the stimulation intensity that is adequate to produce activation of the neural tissue. Afterdischarges are nerve impulses that occur after stimulation, and the presence of afterdischarges indicates that the maximum amount of current that can be safely applied to the cortical surface has been reached. Monitoring for the presence of afterdischarges using electrocorticography (ECoG) is necessary to avoid the complication of seizure during cortical stimulation and also provides a measure of the adequacy of stimulation (see Chap. 10).

In situations where surgery needs to be performed to remove cerebral tissue, such as for tumor resection, or when an incision must be made through this more superficial cerebral tissue to get access to a deeper structure, a specific determination of the areas of the patient's brain controlling a specific function becomes important. Likewise, it is also important to know where the "silent" areas are that surround these functions. The surgical goal may be to affect a particular cortical area or to specifically avoid affecting a few or many of these cortical areas.

Within this context, identification of "eloquent cortex" becomes quite important. Eloquent cortex is a term used by neurologists and neurosurgeons for areas of cortex that result in a loss of sensory processing or linguistic ability or some degree of loss of sensory or motor function if it is damaged or removed. These defined areas of cortex are crucial for certain particular functions, and some areas are indispensable for a particular cortical function [6]. The most commonly recognized areas of eloquent cortex are in the left temporal

and frontal lobes, i.e., Broca's and Wernicke's areas (speech and language); bilateral occipital lobes (vision); bilateral parietal lobes (sensation); and bilateral motor cortex (movement).

Cortical mapping may also be done to attempt to identify an epileptogenic focus so that surgical excision or ablation of that area can be accomplished. The goal of complete resection of an epileptogenic focus must often be limited by sparing of eloquent cortex in order to avoid new and unacceptable deficits following epilepsy surgery. Although the homunculus diagram can provide a general idea of where specific motor or sensory functions are likely to be found in the cortex, intraoperative brain mapping provides much more specific information for a particular patient at that specific time of the surgical procedure. As suggested earlier, there are two broad areas of neurosurgery in which intraoperative cortical mapping is employed: excision of intracranial tumors and surgery to treat seizures.

Indications

Application in Cortical Tumor Excision

As already noted, anatomic appearance does not clearly and precisely identify areas of cortical brain tissue subserving a particular function. Multiple studies have shown that long-term prognosis is improved by more extensive tumor excision [7–10]. The use of intraoperative cortical mapping by electrical stimulation of specific anatomical areas provides the neurosurgeon with a "real-time" functional map. When using cortical mapping to identify eloquent cortex for tumor excision, the concept of positive mapping in contrast to negative mapping also comes into play.

A positive mapping occurs when eloquent areas are identified around the site of planned tumor excision. In other words, specific stimulation sites result in a recognized sensory or motor activity, and these sites are in close proximity to the area of resection of the neural tissue. A negative mapping occurs when electrical stimulation of a surrounding area does not produce any recognizable motor or sensory activity [11–13].

Although it would be easy to think that a positive identification of an area subserving a particular motor or sensory function would be desirable, and would allow the surgeon to more precisely navigate the resection around it, experience has shown exactly the opposite. A negative mapping result around eloquent areas seems to provide a better "safe margin" for tumor resection with a low incidence of postoperative neurological defects [14]. In fact, positive identification of eloquent areas around the planned site of tumor resection actually increased the risk of postoperative deficits, probably indicating close proximity of tumor to functional cortex.

Application in Epilepsy Surgery

ECoG is employed in epilepsy surgery in an attempt to identify and remove the "epileptic zone" of tissue. This "epileptic zone" is felt to be the anatomical site of seizure onset as well as the surrounding tissue which might potentially be recruited into the critical mass of tissue involved in the seizure. Although this technique essentially records the same type of electrical activity as an EEG, the electrode montage being placed directly onto the brain tissue, there is less attenuation and dispersion of the electrical signals. This is felt to provide more precise localization of the aberrant electrical activity causing the patient's seizures than a diagnostic EEG.

ECoG requires the presence of a neurophysiologist interpreting the data in real time. Unlike other aspects of intraoperative monitoring, this cannot be accomplished through remote monitoring or telemedicine. The neurophysiologist must remain in close communication with the surgeon. A standard 16-channel EEG machine can be used to do the recording, but since the electrodes are directly on the brain, modifications from the normally used EEG settings of the recording sensitivities, time constants, filters, etc. are made. The machine is usually present in the operating room itself or in an operating room gallery with a two-way communication system in place so that the surgeon and neurophysiologist can communicate.

In order to accurately locate the epileptogenic area, the recording electrodes should be placed at

equal distances from each other, both horizontally and vertically on the cortical surface. Angulated electrode placement should be avoided, since this can lead to false localization. Montages should contain at least four electrodes in a straight line.

Actual ictal events are rarely recorded. Instead, usually only interictal epileptiform activity is noted intraoperatively. The area of maximum epileptiform activity is felt to be the irritative zone that initiates the seizure, but this is not necessarily the area of origin of the epileptic seizure. Alacorn et al. found that removal of this area of maximal epileptiform activity yielded a better chance of good surgical outcome with reduction in epileptic activity, but if the area of maximal discharging was not completely resected, surgical outcome was likely to be poor.

Electrical stimulation of a suspected cortical area has been attempted but without good results in localizing the area of epileptogenic activity. When the stimulated area correlates with eliciting the typical aura preceding the seizure and this coincides with the area of greatest epileptic discharge, there seems to be a better correlation with successful surgical treatment of the seizure activity when that area is resected. However, if afterdischarges occur, the correlation to the epileptic zone is not as strong. This is probably due to afterdischarges originating from a distant and uninvolved area.

After surgical resection, sometimes residual spiking activity will occur. Unfortunately, the significance of this is not clear. While 75 % of patients who were not seizure-free following resection had residual spikes noted on electrocorticography, 36 % of patients who were seizure free following surgical resection also exhibited residual spikes [15].

Anesthetic Considerations

Most anesthetic agents affect electrocorticography. So, for ideal intraoperative monitoring, the most reliable monitoring results when little if any anesthetic agents are used. Today's anesthesiologists have at their disposal multiple short-acting medications that can be used for sedation, analgesia, or inducing general anesthesia. This coupled with airway technologic advancements has made intraoperative control safe and easy for most patients. Because of this progress, many cases with intraoperative cortical mapping are anesthetized using the "asleep–awake–asleep" technique. This allows the patient to be awake, during the surgical procedure on the eloquent centers of the brain, thus allowing the surgeon to monitor the neurological status of the patient and maximize surgical resection. This technique is more commonly used during procedures such as speech mapping and epilepsy surgery when feedback from the patient is most important. Mapping of primary sensory and motor areas is generally not performed with an awake craniotomy as EMG monitoring can be done with the patient asleep thereby minimizing patient stress, airway complications, and coincident seizures.

General Anesthesia

For sensorimotor mapping with the patient under general anesthesia, a total intravenous anesthesia regimen using propofol and narcotics is preferred. Neuromuscular blockade should be avoided. This regimen preserves the specificity of motor mapping while reducing the incidence of seizures in response to cortical stimulation. Although the use of propofol reduces the incidence of seizures, it does not eliminate the risk, and the team should be prepared to treat an intraoperative seizure if it occurs. The placement of bilateral soft bite blocks (as would be done for MEP monitoring) is also important.

Awake Craniotomy

A successful intraoperative course for an awake craniotomy starts with the preoperative evaluation. Medications should be noted, as well as concurrent medical conditions and serum levels of any antiseizure drugs currently being taken. A history of complications from medical management of seizures should also be discussed.

The patient should be given a detailed account of expected intraoperative events and warned of

certain intraoperative events, such as opening the dura that may cause some discomfort. The anesthesiologist must reiterate the advantages of the patient being awake and ensure the patient that he/she will be present throughout the operation minimizing anxiety and pain when possible. Therefore, constant intraoperative communication with the neuroanesthesiologist will be expected. Lastly, induction and emergence from anesthesiology should be discussed with the patient.

Intraoperative: Local Anesthetics

Intraoperatively, the anesthesiologist and neurosurgeon use local anesthesia to perform regional, field, and dural blocks. Cutaneous nerves branching from the trigeminal nerve innervate the skin, scalp, pericranium, and periosteum. Subcutaneous infiltration with lidocaine or bupivacaine with epinephrine is commonly employed and successful in blocking afferent input to these areas. The skull has no sensory innervation, so it can be drilled and opened with no patient discomfort. The dura receives innervation from all three divisions of the trigeminal nerve, the recurrent meningeal branch of the vagus, and by branches of the upper cervical roots and can produce significant discomfort for the patient when instrumented by the surgeon. Local application by the surgeon can work; however, if this becomes too unpleasant for the patient, then general anesthesia can be induced and a laryngeal mask airway inserted until exposure is completed.

Intraoperative Sedation

Current techniques commonly use propofol, fentanyl, remifentanil, or dexmedetomidate. Many use propofol infusions with slow and careful titrations of fentanyl. Most recently remifentanil has replaced fentanyl due to its ultrashort action and is combined with propofol to provide sedation and analgesia during awake craniotomies. This technique is popular because of the safety profile and lack of respiratory depression if carefully titrated. Dexmedetomidate, an alpha-2-adrenoreceptor agonist, has gained popularity due its ability to provide analgesia and sedation, which is easily reversed with oral communication. Additionally, it produces no respiratory depression when used alone. Ensuring sedation and analgesia for the patient while preventing apnea or airway obstruction is the main concern for the anesthesiologist. Airway equipment (oral and nasal airways, laryngeal mask airways, and emergency intubation equipment) must be readily available throughout the case.

Asleep–Awake–Asleep Technique

Propofol and remifentanil are the two agents used most frequently for this technique. Both are short-acting, safe, and predictable. Additionally, they can be titrated while using the bispectral index monitoring system, which provides the anesthesiologist more precision for drug dosing adjustment. A laryngeal mask airway is commonly inserted to prevent airway obstruction. With proper propofol and remifentanil dosing, airway irritation is alleviated and neuromuscular blocking agents are not warranted. After the craniotomy is completed and the dura is opened, the remifentanil dose is reduced or stopped, and spontaneous respirations are allowed to resume. The propofol infusion is reduced, and the LMA is removed as the patient regains consciousness. After surgical resection is completed, the infusions are reinstated and the LMA placed until surgery is completed.

Contraindication to Awake Craniotomies

Multiple issues must be considered before proceeding with an awake craniotomy. The ability to communicate with the surgeon and anesthesiologists is imperative. Any communication problems, such as dysphasia, are strong contraindications for awake craniotomies. Extremely anxious patients or patients prone to an exaggerated pain response should probably be avoided as are patients requiring prone positioning for surgery. Patients with

lesions requiring extensive dural surgical resection should probably be avoided. Finally, lengthy surgical procedures may make it difficult for patients who are required to lie still.

Conclusion

It is now recognized that the area of the brain responsible for written and verbal communication varies with each individual. To fully understand the impact of surgical resection, the surgeon should insist on intraoperative cortical mapping. When intraoperative cortical mapping is employed, the surgeon can maximize surgical resection and minimize postoperative disabilities for the patient. Advancements in anesthetic pharmacologic agents and anesthetic equipment have allowed patients to undergo mapping and resection with minimal discomfort while being awake and continuously checked for neurologic interval changes.

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Neurological Assessment and Correlation in Spinal Cord Nerve Root Pathology

19

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In order to perform an adequate neurological assessment of a patient, one must combine a thorough history and physical with other diagnostic studies. When patients present with neurological symptoms such as weakness, pain, or numbness and tingling, the clinician needs to perform a detailed examination to determine if a neurological deficit actually does exist. Sometimes more than one component of the neurological system may be affected. It is important to note that while the sensory cell body of the nerve root lies within the dorsal root ganglion and is extraspinal, the cell body of the motor nerve root is the anterior horn cell that lies within the spinal cord which is intraspinal. This chapter will emphasize spinal cord nerve root pathology and the role of the clinician in identifying aberrant states.

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History

Patients may complain of weakness, pain, or numbness and tingling in one or more extremities. Important points to discuss with patients during their initial visit include the location and character of their symptoms, how and when it started, if there are any exacerbating or relieving factors, whether it is continuous or intermittent, and how certain position affects the symptoms. Psychosocial factors can also play a significant role in how patients experience pain. Therefore, it is necessary to also ask questions about how stress affects the pain, whether there is a concomitant sleep or mood disorder, how pain affects the patient's function at work or school, and how the pain affects quality of life. Furthermore, a patient's motivation for evaluation must be clarified early. If there is possible litigation involved, it can affect how patients portray and describe their pain.

Physical Examination

The physical examination begins as soon as the patient walks in the door. Clinicians will take note of how patients walk, sit down, get up, and what their posture is like. Whether a patient exhibits ataxia, walks with a limp, or must use a cane or walker to ambulate provides important information. Take note of the patient's overall appearance, including weight and muscle bulk,

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masses, and signs of injury. Are there differences in the skin, nails, hair, and temperature of the limbs? Look at the spine for the presence of scoliosis, kyphosis, and loss of curvature.

Motor Examination

There are several steps that make up the motor examination. With each assessment, it is important to compare the left and right sides. First, the examiner should observe the patient to detect any signs of a movement disorder, such as twitches or tremors, which are usually associated with lesions of the basal ganglia and cerebellum. The patient's posture when he or she walks into the room and sits down should also be noted. An abnormal position may be indicative of weakness. The examiner also inspects the muscles for signs of wasting or hypertrophy, which can be followed by measuring the circumference at a specific location. Additionally, the examiner may palpate muscles to detect any tenderness. Muscle tone is tested by instructing the patient to relax while the examiner passively moves a joint through normal range of motion, feeling for any rigidity or flaccidity.

It is important to distinguish actual muscle weakness from pain-limited strength and lack of effort. A specific pattern of weakness can help to localize a lesion. Many clinicians will test a muscle group on one side of the body and then test its contralateral counterpart to enhance detection of any asymmetries. It is also important to be aware of differences in proximal and distal muscle strength. In general, muscles do not work in isolation, and therefore, the scale really is better used in order to describe a motion per se, rather than an isolated muscle. For example, elbow flexion versus biceps strength. At any rate, muscle strength is usually rated on a scale of 0–5 (Table 19.1).

Table 19.1 Muscle Strength Grading Scale

0	No muscle contraction
1	Slight contraction but no movement
2	Movement is possible when gravity eliminated (test in horizontal plane)
3	Movement is possible against gravity but not against resistance; moderate weakness
4	Movement against gravity and some resistance; slight weakness
5	Full range of motion against gravity and resistance; normal strength

While muscles often work in synergy to create in aggregate a given motion, they rarely work in isolation. Nonetheless, to test the deltoid muscles, which are innervated primarily by the C5 nerve root and to a lesser extent the C6 nerve root, patients simultaneously raise both arms in front of them as the examiner provides resistance to this movement. The biceps muscles are innervated by the C5 and C6 nerve roots. To test the strength of the biceps, hold the patient's wrist from above and provide resistance and instruct him or her to flex the hand up to the shoulder. Next, test the triceps muscle strength. Patients should start from a fully flexed position and extend their forearm against resistance provided by the examiner. The triceps muscle, the major elbow extensor, is primarily innervated by C7 nerve roots and to a lesser extent a C6 and a C8 (long head of the triceps) component. Wrist flexion is predominantly C7 and to a lesser extent C6 can be tested by having the patient flex their wrist. Wrist extensors are innervated predominantly C6 and to a lesser extent C7 nerve roots can be tested by having patients extend their wrists while the clinician is providing resistance. Examine the patient's hands for signs of thenar and hypothenar muscle wasting. To test grip strength, ask patients to make a tight fist around the examiner's fingers and instruct them to not let go as the examiner tries to remove them. Grip strength is a test of intrinsic hand muscles and finger flexion, which is innervated by the C8 nerve root. Thumb abduction, which is primarily innervated by the T1 nerve root, is tested by having patients abduct the thumb. Thumb opposition is innervated by the C8 and T1 nerve roots and is tested by having patients touch the tip of their thumb to the tip of their pinky finger as the clinician is applying resistance to the patients' thumb.

Hip flexion is tested by having the patient lie supine and raising each leg separately as the examiner is providing resistance. Hip flexion is

innervated by the L2 and L3 nerve roots and tests the iliopsoas muscle. The L2, L3, and L4 nerve roots provide innervation for adduction of the hip. Hip adduction is tested by the examiner placing his or her hands on the inner thighs of the patients and instructing them to bring both legs together. The gluteus maximus and gluteus minimus muscles are tested by having the examiner's hands on the patient's outer thighs and providing resistance while the patients move their legs apart. Innervation for this movement comes primarily from L5, and S1 nerve roots, and to a lesser extent the L4 nerve root. Extension of the hip is tested by having the patient lie supine with one leg raised, the examiner placing a hand under the patient's thigh, and then instructing the patient to press down on the examiner's hand. This tests the gluteus maximus, and innervation comes primarily from the L5 and S1 nerve roots. The L3 and L4 nerve roots provide innervation for knee extension by the quadriceps muscle. Extension at the knee can be tested by the examiner placing a hand on the anterior surface of the lower leg to provide resistance and having the patient "kick out." This movement tests the quadriceps muscle, and innervation is provided by the L3 and L4 nerve roots. The hamstring muscles are innervated by the L5 and S1 nerve roots, which allow for flexion at the knee. Test flexion at the knee by placing a hand on the pack of patients' calves and instructing them to pull the lower leg back. Dorsiflexion of the ankle is tested by placing a hand on top of the ankle and having patients pull their foot up towards their face as the examiner is applying resistance. This tests muscles in the anterior compartment of the lower leg, and innervation comes primarily from the L5 and sometimes the L4 nerve root. Next, hold the bottom of the patient's foot to provide resistance and instruct them to "step on the gas pedal" to test the gastrocnemius and soleus muscles. This ankle plantar flexion receives innervation from the S1 and S2 nerve roots. To test the extensor hallucis longus muscles, which are innervated by the L5 nerve root, ask the patient to move the large toe up towards the patient's face while providing resistance.

Table 19.2 Deep Tendon Reflex Grading Scale

0	No response; abnormal
1+	Trace response; may or may not be normal
2+	Average response; normal
3+	Very brisk response; may or may not be normal
4+	Clonus; always abnormal greater than 2 beats

Deep Tendon Reflexes

When a muscle tendon is tapped, the muscle will normally immediately contract. Hyperactive or clonic reflexes (3+ or 4+) are suggestive of an upper motor neuron lesion consistent with a disruption in the descending corticospinal tract or at a higher level. Hypoactive reflexes (0 or 1+), on the other hand, can be caused by lesions in lower motor neurons, muscles, sensory neurons, and neuromuscular junctions. Arthritis or any contracture of a joint can mechanically lead to diminished reflexes. The grading scale for deep tendon reflexes (DTRs) is shown in Table 19.2.

The biceps reflex tests the C5 and C6 nerve roots. The patient's arm is partially flexed at the elbow, and the examiner places a finger over the biceps tendon and then strikes his or her finger with a reflex hammer. The brachioradialis reflex also tests the C5 and C6 nerve roots. Position patients with their arm bent at the elbow and resting on their thigh. When the tendon is struck approximately 3 in. proximal to the wrist, the muscle will contract and the arm will supinate. The pronator teres reflex, which reflects the C7 nerve root level, is tested with the elbow bent at 90°. The forearm is positioned at a neutral position and the distal radius is tapped anteriorly, eliciting a reflex response. To test the triceps reflex, which is mediated by the C7 and C8 nerve roots, the clinician can hold the patient's arm at the antecubital fossa and instruct the patient to let the arm hang loosely 90° at the elbow. The examiner then strikes the tendon proximal to the olecranon. The normal response is contraction of the triceps muscle with extension of the elbow. To reinforce testing of deep tendon reflexes in the upper extremities, the examiner may ask the patient to clench their teeth. This maneuver will

distract patients in the case of the examiner having difficulty eliciting reflexes.

There are two deep tendon reflexes in the lower extremity that are commonly tested—patellar and Achilles. The patellar reflex ("knee jerk") is mediated via the L3 and L4 nerve roots. The patellar tendon is usually visible and palpable below the kneecap. The patient should be sitting on the edge of the examination table with the lower leg hanging freely, and when the tendon is struck, the normal reflex is for the quadriceps muscles to contract, causing extension at the knee. The hamstring reflex can be used to test the L5 nerve root level. The patient lies on their side with the knee flexed 90°. The medial distal hamstring tendon is tapped to elicit a response. The S1 and S2 nerve roots mediate the Achilles reflex ("ankle jerk"). To elicit this reflex, the patient's lower leg should be hanging freely over the edge of the examination table and the examiner should hold the foot at 90°. Striking the tendon with the reflex hammer should cause contraction of the gastrocnemius muscle and plantar flexion of the foot. The Jendrassik maneuver helps to reinforce testing of deep tendon reflexes in the lower extremities. This is accomplished by having patients flex all of their fingers, hook them together, and pull apart.

Sensory Examination

The sensory examination of the extremities assesses the spinothalamic and dorsal column afferent pathways. The spinothalamic tract consists of nerves that detect pain, temperature, and crude touch. The nerve fibers course from the periphery to the spinal cord, where they cross over to the other side within one or two vertebral levels of where they enter. The fibers then continue their course up to the brain and synapse in the cerebral hemisphere on the opposite side of the body from where they originally began. To test a patient's ability to sense sharpness, many clinicians will break a cotton swab in half to create a sharp end. Ask patients to close their eyes so as to not allow them to be distracted by visual clues.

Table 19.3 Dermatomal sensory distribution

Posterior aspect of shoulders	C4
Lateral aspect of upper arms	C5
Tip of thumb	C6
Tip of 3rd digit	C7
Tip of 5th digit	C8
Medial aspect of lower arms	T1
Upper and lateral part of thigh	L2
Lower-medial aspect of thigh and patella region	L3
Medial leg	L4
Lateral leg and first toe	L5
Sole of foot and the fifth toe	S1

Alternate touching the patients with the sharp end and the cotton end in specific dermatomes, and ask them to state whether they are feeling a sharp or dull sensation. Patients should also note if they experience a difference in sensation on each side of the body. To test particular dermatomes, the examiner should touch the patient in the areas shown in Table 19.3.

Temperature sensation is also carried by the spinothalamic tract. In the office setting, this is often done with a metal object, which feels cold on the skin. As with testing for sharp sensation, touch the patient at specific dermatome areas. The findings on this examination should corroborate those of the sharp stimulus testing.

Proprioception and vibration sense are mediated through the dorsal columns of the spinal cord. Unlike the nerve fibers of the spinothalamic tract that cross over to the contralateral side, the nerves of the dorsal columns course up the spinal cord on the same side, and then course over at the brainstem. Proprioception is the ability of the body to know where it is in space, which aids in the ability to balance. The examiner can test proprioception by holding the patient's big toe on the sides, moving it either up or down, and asking the patient which position it is in. The patient's eyes should be closed during this maneuver so as to not receive any visual hints. If the patient is not able to correctly identify the position of the toe, then the examiner should move more proximally, such as to the ankles, and repeat the test. Similar testing may also be done in the upper extremities at the fingers, wrists, and elbows.

Vibratory sensation is also mediated by the dorsal columns of the spinal cord, so the results should verify the findings of the proprioception testing. Generally, the examiner starts by having the patient seated and places a vibrating tuning fork on top of the interphalangeal joint of the great toe and also places two or three fingers from the other hand on the bottom side of this joint. The examiner should be able to feel the vibrations transmitted through the joint with his or her fingers. The patient should be able to determine when the vibrations cease, which the examiner should also be able to feel.

Nerve roots can be damaged as they branch off from the spinal cord. For example, herniated disc material or tumors can compress the nerve roots, which will result in a sensory deficit in its distribution. The examiner should be able to identify the deficit on examination. The sensory examination can be altered by the presence of diabetes mellitus, thiamine deficiency, and neurotoxin damage.

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Electrophysiological Assessment of Spinal Cord Pathology in Pain Medicine

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Keri D. Copponex, Alan David Kaye, Joseph H. Feinberg, and Megan A. Frantz

Although there are some newer radiologic imaging methods available, electrophysiological tests remain useful in the assessment of both central and peripheral nervous system dysfunction. Electrophysiological tests can provide information that radiographic studies like magnetic resonance imaging (MRI) cannot provide, such as the severity and chronicity of a neurological problem. These tests are also helpful in establishing whether an abnormality seen on radiographic images is even clinically significant. On the other hand, electrophysiological tests can detect abnormalities not seen on radiographic images.

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Nerve Conduction Studies

Motor Nerve Conduction Studies

The basis of motor nerve conduction studies is that a nerve is electrically stimulated and multiple parameters are measured to determine how well the nerve transmits an impulse. To do this, one electrode is placed over a muscle and a second electrode is placed over the tendon insertion of that muscle. The examiner stimulates the nerve at a certain distance from the muscle and the evoked response is recorded. The latency is the time from stimulation of the nerve until the evoked response, which represents depolarization of the muscle, occurs. Then the examiner will stimulate the nerve at a more proximal site, and the latency at this site is also determined. The velocity of conduction between these two points is calculated by dividing the distance between them by the difference between the latency of the distal stimulation site and the latency of the proximal stimulation site. The conduction velocity from the distal stimulation site to the muscle cannot be determined, though, because of intrinsic delays at the neuromuscular junction [1].

The F wave is also measured in motor nerve conduction studies. When a nerve is stimulated, the axon depolarizes not only distally, but also proximally. The distal depolarization causes the evoked response discussed above, while the proximal depolarization travels to the spinal cord via antidromic conduction of alpha motor neurons. Anterior horn cells are then activated, and the

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impulse travels orthodromically to depolarize the muscle, which is the F response. The F response can be variable and is a test of motor function only. They are helpful in determining if there is a disturbance in the function in the proximal nerve. For example, if distal nerve conduction studies are normal but the F wave latency is prolonged, there may be a lesion of the proximal nerve [2].

Sensory Nerve Conduction Studies

An active electrode and a reference electrode are placed over the nerve being studied, and the nerve is stimulated either proximally or distally to the electrodes. If stimulated proximally, antidromic conduction occurs, and if stimulated distally, orthodromic conduction occurs. The time from the onset of the stimulus to the onset of the action potential is measured and is divided by the distance between the two electrodes; this value represents the sensory conduction velocity [3].

When the nerve conduction velocity is decreased, it is usually due to a disorder of the myelin, but may also be seen in disorders affecting larger axons. Dysfunction of the axons more commonly causes a decrease in the amplitude of evoked motor and sensory responses because fewer fibers are able to conduct the response [3].

Reflex Studies

In reflex studies, a sensory nerve is stimulated and a motor response is recorded and measured. The H reflex is often described as the electrical counterpart to the muscle stretch reflex of the ankle jerk. The posterior tibial nerve is submaximally stimulated at the popliteal fossa to selectively depolarize the large Ia afferent fibers. The impulse is carried to the dorsal horn of the spinal cord, where it then depolarizes alpha motor neurons in the anterior horn. The impulse travels back to the soleus muscle and causes it to contract. Consequently, the H reflex helps to determine the integrity of both the S1 motor and sensory nerves. While it is most common to evaluate S1 radiculopathies, H reflex testing has also been used to assess C6–C7 lesions by stimulating the median nerve and measuring the response at the flexor carpi radialis muscle, and also L3–L4 lesions by stimulating the femoral nerve and recording from the vastus medialis muscle [3]. The amplitude of the H reflex is increased after spinal cord injuries. H reflexes are still present during spinal shock even though deep tendon reflexes are lost.

Electromyography

Electromyography evaluates and records electrical changes within a skeletal muscle. In the resting state, muscle fibers have a transmembrane potential of 70–90 mV. The inside of the cell has a negative charge versus the outside. When a nerve impulse reaches the neuromuscular junction, acetylcholine is released and initiates an action potential that spreads across the muscle fiber and causes contraction. A monopolar needle electrode is commonly used to perform electromyography. It is a wire electrode coated with insulating Teflon, sparing the tip because that is where the recording occurs. The small-diameter needle is inserted into the muscle and there is a surface electrode on the patient's skin. The needle is attached to an oscilloscope with an amplifier, so electrical activity of the muscle can be observed as waveforms, and the examiner can also hear the characteristic sounds of various potential changes encountered.

The examiner will evaluate spontaneous activity of the muscle by instructing the patient to relax the limb as much as possible. Insertional activity is the response that occurs when the needle is inserted into the muscle. A burst of spike potential occurs up to 100–300 ms after the conclusion of needle motion. A prolonged time of insertional activity can be a sign of neuromuscular disease, while a decreased insertional activity time may indicate loss of muscle tissue. There is normally no electrical activity in resting muscle. However, there can be normal spontaneous activity if the needle electrode is near a motor end plate. Abnormal spontaneous activity includes fibrillation potentials and positive sharp waves,

which are seen if the muscle fiber membrane is electrically unstable. Fibrillations occur when the muscle fiber loses continuity with its motor nerve, thus allowing for spontaneous depolarization. They are associated with lower motor neuron diseases such as radiculopathies, neuropathies, and anterior horn cell pathology, as well as myopathies, hypokalemia, and hyperkalemia. Fibrillations have been reported in cases of spinal cord injury as well, though this is controversial [3]. Positive sharp waves are associated with the same disorders as fibrillations.

Somatosensory Evoked Potentials

Somatosensory evoked potentials (SSEPs) are a technique to evaluate the function of the ascending spinal tract. They are obtained by stimulating a peripheral nerve, usually the median or ulnar at the wrist or the tibial or peroneal at the ankle, and recording the response from the patient's scalp. They are often used intraoperatively to monitor spinal cord function. SSEPs can evaluate the function of the distal and proximal peripheral nervous system, as well as the spinal cord and brain, since the potentials are carried by sensory nerves peripherally and by the dorsal column-lemniscal system centrally. They have been reported to be of some use in determining ambulation outcomes [4]. Iseli et al. discovered that patients with ischemic spinal cord injury had similar motor and sensory deficits as patients with traumatic spinal cord injury. Both groups also had pathological SSEP recordings [5].

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Spinal Cord Stimulation: Principles and Applications

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Ramsin Benyamin, Jay S. Grider, Ricardo Vallejo, Dana M. Tilley, and Alan David Kaye

The concept of electrical stimulation applied to the treatment of pain was first documented in a book published in 47 AD called the *Compositiones* by Scribonius Largus. Largus demonstrated that shock incurred by the torpedo ray induced analgesia for both gout and headaches. A substantial amount of progress has occurred since that time, providing treatment for a wide range of clinical symptoms using various electrical stimulation modalities. There are two clinical applications for electrical stimulation to nerves. The first is designed to treat motor disorders such as tremors caused by advanced Parkinson's Disease. The more common use for electrical stimulation uses focused electrical treatment to neural targets resulting in analgesia. Current targets for stimulation include the spinal cord, dorsal root ganglia, and peripheral nerve tracts.

The predominate use of electrical stimulation is spinal cord stimulation (SCS), where direct electrical stimuli is applied to the spinal cord for the treatment of chronic pain. This concept is based on gate control theory by Melzack and Wall [1]. This theory dictates that the stimulation of large beta fibers closes the gate on small fiber transmission resulting in perceived analgesia.

Shortly after gate control theory was introduced, electrical stimulation for the treatment of pain progressed rapidly with the introduction of new devices and applications. In 1967 Wall and Sweet used infraorbital stimulation for the first time. Later that year, the first spinal cord stimulator was implanted by Shealy and Mortimer. One year later, in 1968, Sweet and Wepsic implanted the first peripheral nerve stimulator. The first commercial spinal cord stimulator was introduced by Medtronic in that same year. The standard non-rechargeable batteries were replaced by the first rechargeable battery in 2004 by Advanced Bionics which later became part of Boston Scientific.

Currently, neuromodulation has three primary manifestations: spinal cord stimulation, peripheral

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nerve stimulation, and intracranial stimulation of the deep brain and motor cortex. There are two major advantages to these therapies: reversibility of treatment and treatment trial prior to permanent implant. The trial of the device allows the patient to test the treatment in a more minimally invasive manner to determine efficacy. The technical goal is to obtain overlap of electrical stimulation on painful areas. The clinical goals are reduction in pain, improved function and quality of life, and reduction in the amount of analgesic pain medication. Indications for the device in the USA are failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). Indications for the device in Europe are ischemic pain caused by peripheral vascular disease and intractable angina.

Spinal cord stimulation is a useful therapy in the treatment of a multitude of pain conditions. A literature review of SCS in FBSS patients revealed that SCS is effective in relieving the chronic intractable pain associated with the syndrome [2]. This type of neuromodulation is also reported to be effective in certain applications for discogenic pain and Reynaud's syndrome by altering sympathetic outflow, resulting in increased blood flow and decreased pain [3]. Neuromodulation is a promising treatment for long-term chronic and neuropathic pain modalities.

Physiology and Biophysics of Neuromodulation

Understanding the physiology behind SCS requires review of basic neurologic functioning at both the cellular and axonal level. Recall that each axonal cell body in the inactive state has a negative resting potential. Upon activation of the axonal cell body, the inward sodium current increases the resting potential to the threshold potential. Once the threshold potential is reached an action potential is initiated. This action potential propagates down the axon via salutatory conduction in myelinated axons. However, the basic transduction of the signal from the spinal cord stimulator electrode to the biological system is often poorly understood.

In order to better comprehend this concept, conduction of electrical signals in nonbiological systems must be understood. In nonbiological systems, electrical current is carried via a conducting medium (in this case the conductive material in the spinal cord stimulator lead). The electrical current in the SCS lead electrode results in the flow of electrons producing an electrochemical reaction. There are two types of electrochemical reactions: galvanic and electrolytic. Galvanic cells *produce* electrical energy while electrolytic cells *consume* energy. In basic terms, the SCS is a galvanic cell while the biological system is an electrolytic cell. The SCS electrodes have non-insulated regions known as "contacts" that provide the interface between the SCS and biological tissue. This contact is programmed to be either positive (anode or oxidative contact) or negative (cathode or reductive contact). By convention electron flow is described as moving from the positively charged anode to the negatively charged cathode. This flow of electrons creates an electrical field. It is the size and "shape" of the generated electrical field that clinicians manipulate to produce the desired clinical result with SCS systems [4].

The conduction of electrons in the SCS lead is a Faradaic reaction. A Faradaic reaction is flow of charge electrical (i.e., nonbiological) systems such as wiring. When the electrical field produced by the flow electrons in this electrical system contacts biologic tissue the energy (galvanic reaction) is converted or transduced into a biological flow of charge. This biologic flow of charge is produced by the movement of the ions in the electrolyte cellular solution and is known as a non-Faradaic process.

For example, an electrode is placed into nonionic water. The water molecules are electrically neutral but do have regions of charge (positive oxygen/negative hydrogen). When the negatively charged (cathode) is produced, the water molecules move to orient themselves with the positive region of the molecule facing the negatively charged electrode contact. In an electrolyte containing solution, the positively charged ions (sodium in the case of the axon) move toward the negatively charged electrons when an electrical

field is generated. This movement of sodium creates a regional charge imbalance which, if occurring at the neuronal membrane, alters the resting membrane potential and activates an action potential. This sequence of events transduces the electrical energy of the SCS into an action potential within the sensory fibers of the dorsal columns of the spinal cord [5]. The resulting sensory activation is felt by the patient and the sensation is described as a *paresthesia*.

This paresthesia, when overlapping the dermatome or region of neuropathic pain, competes with pathologically activated pain pathways within the dorsal horn. Through a complex signal processing and conduction, this sensation reaches the higher brain centers [6]. The dorsal horn acts as a processing station for incoming sensory information. Sensory input such as the sensation of pain and the generated paresthesias are processed simultaneously by the dorsal horn and the representative sensory input is relayed to the cortex [7]. This process is known as signal convergence. Signal convergence within the spinal cord is utilized by SCS to create an analgesic effect [7]. In essence, the presence of a non-noxious paresthesia produced by the SCS system competes with the noxious stimulus from the pain fibers. As described in the gate control theory of pain, this non-noxious stimulus acts to dampen the painful noxious stimulus at the level of the dorsal horn.

Ohm's law governs the properties of the electrical field generated. The components of Ohm's law, voltage, current, and resistance (and the close corollary impedance), are best thought of in terms of fluid dynamics. In this case, voltage is roughly analogous to the force or pressure of water, resistance to the size of the opening through which the fluid moves, and current to the volume of fluid that moves through the opening in a unit of time. Using a garden hose as an example, if the nozzle opening is made smaller (i.e., an increase in resistance) but pressure (i.e., voltage) is held constant, flow or current will decrease. Since the relationship of Ohm's law is $V = I \times R$, when voltage is held constant, an increase in resistance will result in a decrease in flow or current. The other relationships follow similarly.

This is a vital concept, since SCS systems control the (dependent) variables of voltage or current, while resistance (or its close corollary impedance) tends to be a function of the biologic system and, therefore, an independent variable. These considerations are debatable from a clinical standpoint as it is presently unclear if constant voltage or constant current SCS systems provide different clinical results.

Basics of Spinal Cord Stimulator Programming

The electrical field generated and the paresthesia elicited by the electrical field can be customized to patient preference. For example, each "pulsation" or electrical field has an amplitude (or strength of pulsation), a pulse width (how long the pulse lasts), and a frequency rate (pulses per second) (Fig. 21.1). These parameters can be manipulated to alter the perception of the stimulation paresthesia. When a SCS lead is in place over the target tissue, the strength of the pulse is gradually increased until the patient first detects the stimulation. This is called the *perception threshold*.

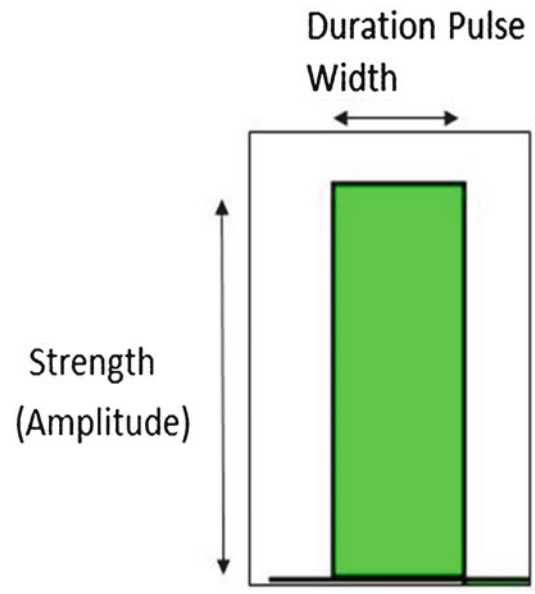

Fig. 21.1 Square pulse commonly used for spinal cord stimulation which is dependent on amplitude and pulse width

The stimulation may be increased to a therapeutic value and ultimately may be increased beyond the ability of the subject to tolerate the sensation. This is referred to as the *discomfort threshold* or the amplitude (strength) at which the patient no longer tolerates the stimulation. It is important during the trial and implantation phase to carefully determine these parameters, as a subject with a very narrow ratio of perception to discomfort thresholds (i.e., narrow therapeutic range) may describe the stimulator as "shocking" them or decrease use due to dissatisfaction with the paresthesia.

The pulse or stimulation rate can be manipulated to create distinct pulses. Settings of the SCS can vary between a low rate or a merging of pulse sensations with higher frequency stimulation. Lower frequencies result in a more distinct, slower pulse, while higher frequencies result in a more continuous, smoother sensation.

Complex mathematical modeling of the impact of these parameters on SCS function has been done. Named for Jan Holsheimer, the concept of mapping out the proper lead positioning and concomitant SCS parameters for optimal effect has become known as Holsheimer mapping [8]. While they are advanced concepts, the mathematical underpinnings of SCS programming are important issues to understand when complex programming is required. Pulse width provides an illustrative example of this concept. For example, if a spinal cord stimulator lead is placed in a more lateral position within the epidural space, a longer pulse width may activate the spinal cord nerve root and cause discomfort. In this scenario narrowing the pulse width may be beneficial.

Electrical Field

The shape of the electrical field created is dependent on the configuration of anodes and cathodes. In a simple system using one anode and cathode, charge flows as described above with very little ability to "shape" the contour of the electrical field (Fig. 21.2). Over the last 10 years the utilization of an electrode combination referred to as a "guarded cathode" has proven useful. This

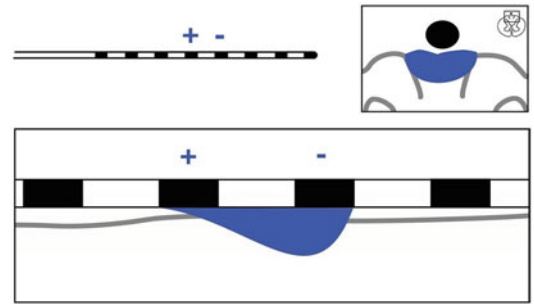

Fig. 21.2 Single anode and cathode configuration

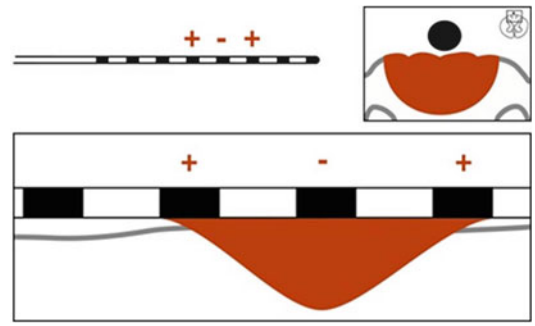

Fig. 21.3 Guarded cathode configuration

configuration has anodes on either side of the negative cathode setting up an electrical barrier to the spread of the electrical field, driving the field in a targeted fashion (Fig. 21.3). This concept is important to successful trialing of SCS as the ability to "steer" current toward the target areas of pain determines the ability to produce the overlapping paresthesia. In the above example the clinical usefulness of driving charge deeper into the spinal cord may be the difference between successfully capturing the desired paresthesia level and an unsuccessful trial.

Technical Aspects of Lead Placement

Pre-placement Planning

Spinal cord stimulation can be utilized at all spinal levels and as such requires some pre-placement planning. For example, cervical leads can be placed at the cervico-thoracic junction or via a

lumbar access site with the lead maneuvered through the epidural space to the cervical target. Both approaches have merit, but different applications. If one is conducting a temporary trial, then the "work" of threading leading leads from the lumbar spine for a patient who may not derive benefit may be futile [9]. Conversely, if the leads are for a permanent implant, the lumbar placement negates the need for lead extensions or extensive subcutaneous tunneling. Similarly if leads are to be placed in the sacral space, a decision must be made whether to attempt placement in a retrograde fashion or via the sacral hiatus.

While there is wide variability among individual patients, there are some guidelines with regard to lead placement targets which may assist the clinician in pre-placement planning. For instance, it is widely accepted that in the cervical spine the C2–C5 region will encompass the shoulder to the arm/hand. Likewise many have observed that obtaining paresthesia coverage for pain in the cervical axial spine is often difficult. Pain of thoracic origin can be broadly categorized as intercostal and visceral. Intercostal paresthesia can often be obtained at or just above the thoracic level of injury in a lateral position, while visceral pain (an area of emerging application for SCS) is currently not well defined and can be highly variable when obtained at all. Paresthesia coverage of pain of lumbar origin is better described. Classic teaching states that the "target zone" for most lumbar pain has an upper limit at T8 level with neurologic mapping undertaken to find the exact location between T8–L1 that works best for a given patient. Lumbar lead placement between L2 (termination of the spinal cord) and L5 is occasionally helpful and has many features in common with nerve root stimulation since the dorsal horn terminates at the T12–L1 level with the conus medullaris (the distal portion of the spinal cord proper at the L1–2 level). Sacral targets, though technically difficult to access, typical are relatively straightforward in their pre-placement assessment in that the effected painful level is typically the optimal site for lead placement.

Physiologic vs. Anatomic Positioning

Regarding "ideal" lead placement, there is considerable variability among individual patients. Many times "ideal" lead placement based on the fluoroscopic images obtained during initial placement (Fig. 21.4) results in nontherapeutic paresthesia patterns, the second image (Fig. 21.4) being the physiologically correct placement for that particular patient. This observation has led to the description of an anatomical midline and a physiological midline or "sweet spot" (Fig. 21.5). This jargon is describing the consistent finding that ideal anatomic position of the SCS lead under imaging (anatomic midline) often requires repositioning of the lead to less aesthetically

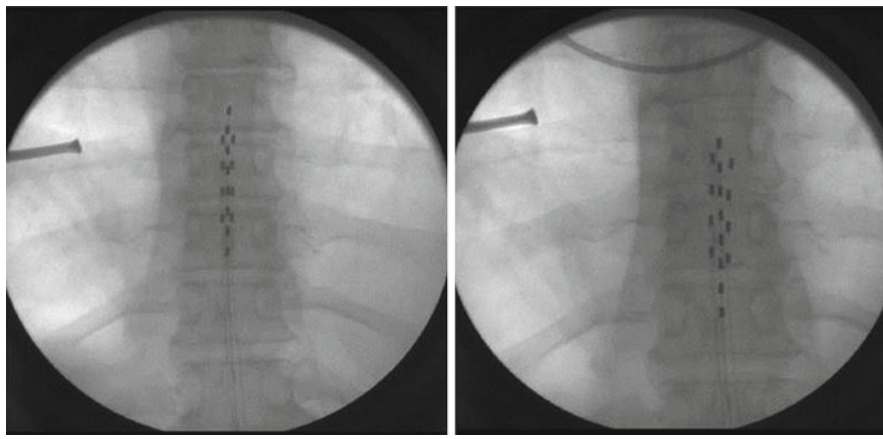

Fig. 21.4 Fluoroscopic image obtained during initial placement (*left panel*) of the "ideal" lead placement and the physiologically correct placement for this particular patient (*right panel*)

pleasing, but more desirable physiologic position to obtain paresthesia coverage of the painful area (physiologic midline). This concept suggests that dorsal column fiber position is variable among individuals, even when the spinal cord is clearly midline on MRI or CT scanning. Another aspect of this physiologic mapping that must be considered is the common observation that one patient may report paresthesia into their feet at T8 while others will experience this same sensation at T10. Further, some individuals, despite meticulous repositioning, never achieve desired paresthesia coverage of the painful area.

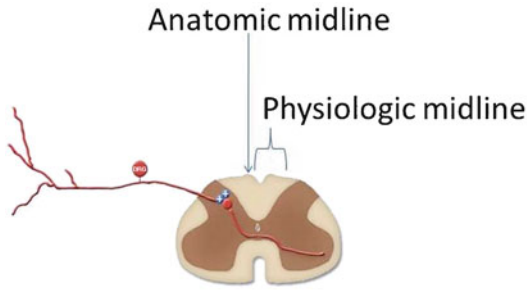

Fig. 21.5 The anatomical midline and the physiological midline or "sweet spot," terms that describe the consistent finding that ideal anatomic position of the SCS lead under imaging (anatomic midline) often requires repositioning of the lead to less aesthetically pleasing but more desirable physiologic position to obtain paresthesia coverage of the painful area (physiologic midline)

Anatomical Conservations

Fiber location within the spinal cord, while also variable, does have some general principles that warrant discussion. Nerve fibers of more distal structures are contained in more central locations within the spinal cord. These fibers become more superficial as they near the exit point within the spinal cord. A spinal cord homunculus analogous to the homunculus at motor cortex has been described that suggests that sacral, lumbar, and thoracic fibers occupy fixed positions within the spinal cord ranging from medial to lateral, respectively (Fig. 21.6). While this concept is widely taught, paresthesia mapping during trialing suggests that the concept of fiber position is of little practical value as the important lead position is the one that has practical clinical value to the patient. Also, it has been reported that nociceptors that innervate the axial spine are

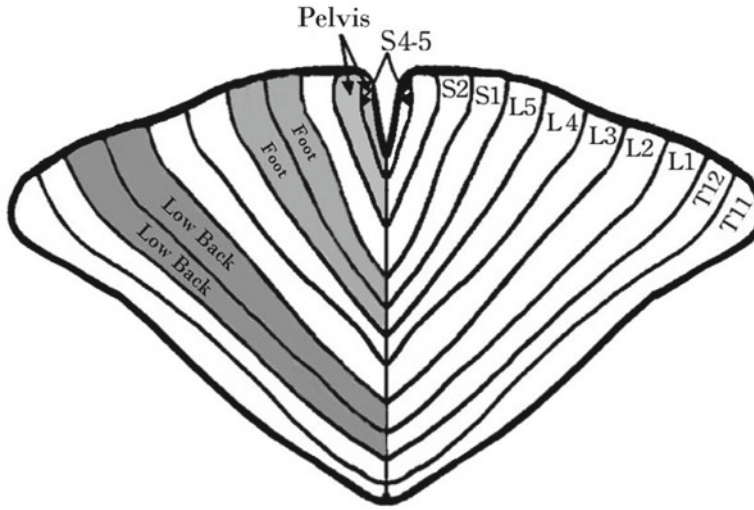

Fig. 21.6 Nerve fibers of more distal structures are contained in more central locations within the spinal cord. These fibers become more superficial as they near the exit point within the spinal cord. A spinal cord homunculus analogous to the homunculus at motor cortex has been described that suggests that sacral, lumbar, and thoracic fibers occupy fixed positions within the spinal cord ranging from medial to lateral, respectively

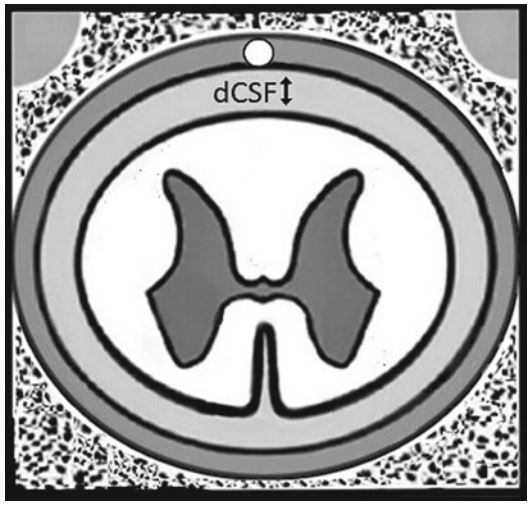

Fig. 21.7 The dCSF thickness varies along the spinal column and can significantly impact stimulation

located at deeper levels within the spinal cord and as such require complex combinations of pulse width and amplitude to achieve penetration to these fibers [10].

Distance between the dura and the spinal cord significantly impacts SCS. The dural cerebrospinal fluid volume varies widely along the length of the spinal cord (Fig. 21.7) and influences the dispersion of current. The CSF levels are maximal at the T5–7 level, which fortunately from a clinical standpoint decrease in the common target zones of C4–6 and T8–L1. The CSF volume at T8–L1 is still significant enough to impact stimulation.

Technical Considerations and Trialing Techniques

Technical Considerations

The number of contacts and leads to be utilized in SCS treatment is a matter of much conjecture and little conclusive evidence. In the mid-2000s, a single or dual 4-contact lead system was the state of the art. A study conducted during this period suggested that there was little advantage in adding a second lead for either radicular lower extremity and/or low back pain [11]. In this study the dual lead system was associated with faster implantable pulse generator (IPG) discharge, without significant improvement in perceived pain relief. Technological advances in IPG battery life coupled with more sophisticated programming options have led to rapid adoption of eight-contact leads which when used in an 8 × 2 array result in all channels of the IPG occupied and available to be utilized [12]. A 16-contact lead has recently entered the market and is already undergoing clinical testing using a 16 × 2 array for enhanced coverage and reducing the need for lead adjustment due to lead migration. The enhanced coverage would only necessitate reprogramming as opposed to additional surgeries.

Leads configured in multiple combinations such as two leads (bipole) and three leads (tripole) have been suggested to enhance coverage of low back pain. This concept is currently under investigation. The introduction of the tripole concept allows the clinician to mimic lead contact coverage obtained with a surgical plate or "paddle" lead [13]. The broad "paddle" lead has wider contact spacing allowing coverage of a wider area within the spinal cord. There also seems to be less lead migration with the paddle lead.

Another advantage over the percutaneous lead lies in the shape of the lead itself. The cylindrical percutaneous lead "radiates" an electrical field in a 360° direction while the surgical paddle lead directs current toward the spinal cord. It has been proposed that this arrangement directs current "deeper" into the spinal cord and may allow better axial back pain coverage. With the multiple contact percutaneous lead the greater contact capability (8 × 1) does allow the clinician to potentially retain paresthesia coverage even if small degrees of lead migration occur [14]. It remains to be seen if the increased number of contact points is of significant benefit from a clinical perspective.

Interleaving

The programming capabilities of multiple contact points allow the programmer to utilize an advanced concept known as *interleaving* to cover multiple areas of pain. The fundamental basis of this approach utilizes the programming of the IPG to rapidly (in microseconds) switch back and

forth between programs on separate portions of the lead that cover different areas of pain. For example in an 8×2 configuration, lead contact 0–4 on a left-sided lead may cover low back pain while 11–15 on the right may cover the radicular lower extremity pain. With rapid cycling between the two areas of lead contact, the patient perceives coverage of both areas. The interested reader is directed to several excellent manuscripts on this topic.

Constant Voltage vs. Constant Current

As discussed previously, all SCS systems are bound by Ohm's law in the way that they transduce the electrical signal to the biological system. If resistance (impedance in these alternating current systems) is relatively constant, and this is dependent upon the biological milieu, the only variables that can be manipulated are voltage or current. The advantages of both approaches can be theoretically debated with excellent arguments emerging for both types of systems. One study has compared constant voltage and constant current in a randomized trial, allowing the patient to determine whether there was a preference between constant voltage and constant current systems. In this small preliminary study, patients could not reproducibly identify constant current systems from constant voltage systems, suggesting that the theoretical differences may not translate into clinically meaningful differences in therapy [15]. This fascinating topic deserves further research.

Spinal Cord Stimulation Trial Techniques

After careful pre-placement planning has been accomplished, it is necessary to plan the trailing process. It is recommended that all patient candidates for SCS should undergo a pretrial psychological assessment to determine if there are unrealistic expectations, secondary gain issues, psychological issues that have not been maximally explored and treated, or other bio-psychosocial factors that may impact treatment success. Once this has been done, it is necessary to discuss with the patient the trialing technique. The purpose of the trial is to temporarily allow the patient to experience the sensation of SCS without having to endure the full implantation process with the IPG. There are two types of percutaneous spinal cord stimulator trials: (1) temporary percutaneous and (2) staged percutaneous placement with permanent anchoring of the leads. Each trialing method has advantages and disadvantages. The more common temporary percutaneous method entails securing the trialed lead to the skin with suture or other easily reversible material in a fashion that is quickly and simply removed. The percutaneous placement with permanent anchoring method requires surgical incision after lead placement and anchoring identical to that which is done with permanent implantation. The anchored leads are then connected to disposable trial connectors and exteriorized via tunneling in an operative setting.

The advantages of the more common temporary percutaneous placement in comparison to permanent anchoring method are (1) easy of placement and removal, (2) can be done in office procedure setting (whereas the surgical anchoring requires a traditional operating suite), (3) less post-procedure discomfort to distract the patient from the trial process, and (4) less invasive. Conversely the percutaneous placement with permanent anchoring results in a more accurate trial to implant experience and less surgical time required for implantation of the IPG [16]. Additionally the IPG placement can be performed under deeper sedation/general anesthesia since sensory mapping is not necessary. Occasionally, the results of the temporary trial are superior to the actual implant using the former method resulting in significant patient dissatisfaction. In the pretrial planning process if it is suspected that spinal epidural access or lead manipulation will be difficult it may be reasonable to do the staged trial with permanent anchoring; otherwise most centers utilized the temporary percutaneous method.

Regardless of trialing method, it is imperative that adequate time with the therapy be given to the patient to determine efficacy. Balancing the need for time with the therapy with the risk of infection usually results in 3–5 day trial period although some clinicians advocate for at

least 7 days [17]. Experience with infection rates of epidural catheters suggests that any trial up to 7–10 represents low risk from an infection standpoint. During the trial, evaluation of functional capacity, sleep hygiene, and pain reduction is key. The person who does not derive functional benefit but claims pain relief should be evaluated closely.

Clinical Indications

While SCS has been utilized for a variety of painful axial and neurological conditions the main indications for the therapy are as follows:

Common Indications:

1. Failed back surgery syndrome: It has been shown that SCS has better outcomes than reoperation. These findings suggest that a trial of SCS before considering a second back surgery should be a part of the treatment algorithm.
2. Radicular pain: Pain of radicular nature in a classic dermatomal distribution in either the cervical, thoracic, or lumbar spine has a relatively strong evidence base suggesting efficacy.
3. Neuropathic pain: Perhaps the strongest indication is the intense pain of neuropathic origin. Entities such as complex regional pain syndrome types 1 and 2, post-herpetic neuralgia, and post-amputation limb pain all respond well to SCS. Of these indications CRPS has strong clinical data to suggest efficacy.
4. Peripheral vascular disease: Such as Raynaud's phenomena, nonoperative limb ischemia, chronic angina, and Berger's Disease.

While these clinical scenarios are well established as responding to SCS there are several exciting areas of emerging application for spinal cord stimulation. Many of these applications have evidence from the case report level to suggest they may improve pain control in patient who has exhausted other possibilities.

These off label applications include:

1. Visceral/abdominal pain: There are case studies to suggest that neuromodulation can successfully be used to improve analgesia for pancreatitis and other pain of visceral origin.
2. Peripheral neuralgia: Spinal cord stimulation technology has been successfully used to treat peripheral nerve pain such as ilioinguinal/iliohypogastric neuralgia and occipital neuralgia.
3. Peripheral field nerve stimulation (PFNS): While still in the emerging stages there is evidence of improvement with pain of myofascial and other origins that is resistant to treatment with subcutaneously placed electrodes. There have been studies published that discuss a cross talk between the epidural and peripherally placed electrodes providing a synergistic effect for resistant peripheral pain syndromes.

Of these applications, peripheral nerve stimulation has strong data to suggest its efficacy while visceral/abdominal applications and PFNS are still in the early stages of description.

Complications

Complications associated with spinal cord stimulation have a low incidence, but they could add significantly to the cost of this treatment. It has been suggested that limiting the number and cost of complications might be the "low lying fruit" that allows us to hold down the cost and maintain access to these treatments [18]. In a systematic review of 22 published reports from 1990 to 2002, a summary of complications in cases of FBSS and CRPS was presented in Pain in 2004 [19]. The authors reported an incidence of 34 % with majority of cases being a revision (Table 21.1) [19]. In the same year, another literature review on efficacy and safety was published that reviewed 51 publications in 20 years including 2972 patients [20]. Of the total incidents recorded, lead migration was the most common adverse event with an incidence of 13.2 %, followed by lead breakage at 9.1 %, infection at 3.4 %, hardware malfunction at 2.9 %, and unwanted stimulation at 2.4 % [20].

Among those reported complications, paralysis was a result of a bacterial infection at the tip of the lead and the skin erosion stopped after removal of the SCS device which was later reimplanted with no adverse events. Additionally, the three patients with hematomas were all on anticoagulation therapies.

Table 21.1 Publications for FBSS and CRPS and concurrent complications in those studies

Author	Year	Classification	*N*	Mean follow-up	% of complications
Probst	1990	FBSS	112	54	29
North et al.	1991	FBSS	50	60	48
De La Porte and Van de Kelft	1993	FBSS	64	48	NA
LeDoux and Langford	1993	FBSS	23	NA	52
Hieu et al.	1994	FBSS	77	42	8
Ohnmeiss et al.	1996	FBSS	40	12	33
McCrory and Keaveny	1997	FBSS	11	20	18
Van Buyten et al.	1999	FBSS	17	28	0
Heidecke et al.	2000	FBSS	42	46	NA
Kavar et al.	2000	FBSS	19	19	21
Villavicencio et al.	2000	FBSS, CRPS	27	31	70
Leveque et al.	2001	FBSS	16	35	81
Alo et al.	2002	FBSS, CRPS	62	48	66
Budd	2002	FBSS	20	60	60
Kumar et al.	2002	FBSS	60	60	NA
Spincemaille et al.	1995	CRPS	11	1	64
Kumar et al.	1997	CRPS	12	41	42
Calvillo et al.	1998	CRPS	24	36	21
Bennett et al.	1999	CRPS	101	NA	14
Kemler et al.	1999	CRPS	18	32	50
Kemler and Furnee	2002	CRPS	24	12	38

Adapted from Turner et al. [19]

Lead migration is the most common complication associated with SCS devices. Lead migration results in a loss of proper paresthesia coverage and a subsequent reduction in pain relief. However, studies show that this is statistically lower in patients with multiple leads or with leads that are multipolar as opposed to monopolar. This is not due to lack of lead migration with the multipolar electrodes but rather the proper paresthesia coverage was most often recaptured by reprogramming. Due to the lack of additional surgeries required to reposition the leads, multipolar leads are the most common implants currently used.

In the case of infections resulting from the implant surgery, these are often treated with antibiotics with the device still implanted though sometimes removal of the device is required before beginning antibiotic therapy. Studies have shown that patients with diabetes are more prone to getting infections and thus have a higher infection rate following SCS implantation.

Occasional cerebrospinal fluid (CSF) leakage may occur after accidentally puncturing the dura with the epidural needle, a guidewire, or the leads themselves during the surgical procedure. A CSF leak can produce headaches, which usually occurs early in the postoperative period. Typically this results in headaches that may be frontal or occipital and accompanied by tinnitus, diplopia, neck pain, and nausea. Small dural punctures typically heal spontaneously and the headache can be treated conservatively. An injection of autologous blood into the patient's epidural space is commonly used to treat a punctured dura that is causing postural headaches if conservative measures are unsuccessful. An overview of complications, diagnoses, and resultant therapies is seen in Table 21.2 [21].

Perhaps one of the greatest unknowns is why SCS has a loss of efficacy over time. These changes may be due to the result of cellular changes in tissue around the electrodes, such as buildup around the contacts, or temporary changes in the electrode positioning such as lead migration or postural changes. There are many reports in the literature of painful stimulation, ineffective stimulation, or loss of stimulation over time. With the

Table 21.2 Overview of complications, resultant diagnosis, and available treatments

Symptomatic diagnosis	Complication	Treatment
Complications within neuraxis		
CT or MRI, Electromyogram/ Nerve Conduction Study (emg/ncs), physical exam	Nerve Injury	Steroid protocol, anticonvulsants, neurosurgery
Increased stimulation amplitude	Epidural fibrosis	Lead programming, lead revision
Physical exam, CT or MRI	Epidural hematoma	Surgical evacuation, steroid protocol
Physical exam, CT or MRI, CBC, blood work	Epidural abscess	Surgical evacuation, IV antibiotics, ID consult
Positional headache, blurred vision, nausea	Postdural puncture headache	IV fluids, rest, blood patch
Complications outside neuraxis		
Serosanguineous fluid in pocket	Seroma	Aspiration, if no response surgical drainage
Blood in pocket	Hematoma	Pressure and aspiration, surgical revision
Pain on palpation	Pain at generator	Lidoderm patches, injection, revision
Fever, rubor, drainage	Wound infection	Antibiotics, incision and drainage, removal
Device-related complications		
Lack of stimulation in area of pain	Unacceptable programming	Reprogramming of device, revision of leads
Inability to program, X-rays	Lead migration	Reprogramming, surgical revision
High impedance, pain at leak site	Current leak	Revision of connectors, generator, or leads
Inability to read device	Generator failure	Replacement of generator

Adapted from Deer et al. [21]

advent of new technologies for electrical stimulation, we are seeing a reduction in complications and enhanced efficacy of stimulation. New technologies are constantly emerging to better shape and define the electric field applied and provide better focused analgesia.

Rare Adverse Effects

Some rare adverse effects of spinal cord stimulation are a direct result of lead placement in the spinal column. Leads placed with the goal of stimulating the caudal segment of the spinal cord can cause micturition inhibition. This unexpected development of neurologic bladder and micturition dysfunction results simultaneously with the onset of pain relief, after the beginning of an electrical stimulation of the caudal segment of the spinal cord (T11–L1) [22]. The interruption of stimulation resolves the symptoms.

Gastrointestinal symptoms are the broadest category of rare adverse side effects. The symptoms range from severe nausea caused by the spinal cord stimulator to abdominal pain and constipation. [23] Constipation and distention are directly related to above paresthesia perceptual threshold. These symptoms often resolve after a period of several weeks and are thought to be related to GI parasympathetic tone or antidromic activation of sensory afferents.

Scar tissue formation is another issue that results in adverse effects. One such issue is cervical cord compression due to delayed scarring around epidural electrodes used in spinal cord stimulation. In a study by Dam-Hieu et al. two surgeries were required to correct this issue [24]. The removal of the SCS alone was not effective. However, the removal of the scar tissue resulted in significant improvement of symptoms. Another, similar complication is late-onset cervical myelopathy secondary to fibrous scar tissue formation around the spinal cord stimulation electrode [25]. A similar case was also reported as Spinal Cord Compression from a Foreign Body Reaction to Spinal Cord Stimulation [26]. An epidural mass

causing significant cervical stenosis and spinal cord compression occurred in one case at the site of a previous SCS. Decompressive laminectomies and a resection of the mass were required.

It is important to understand that these are rare, isolated cases of SCS causing adverse effects. The aforementioned adverse effects are possible in an SCS implant and therefore must be monitored.

Evolving Technologies and the Future of SCS

Spinal cord stimulation originally consisted of monopolar leads connected to external generators to create the electric field around the spinal cord for the treatment of chronic pain. Since then we have expanded to fully implanted rechargeable batteries and leads have progressed from monopolar plates to multiple leads with multiple contacts allowing for up to 32 contacts. More impressive is that each contact has individual power sources to maximize precision targeting of pain. In addition to the continual improvements in technology, the field of SCS has expanded from stimulating only the spinal cord to also being applied to regions of the brain, now called deep brain stimulation (DBS), as well as peripheral nerve stimulation being applied to more peripheral structures like the dorsal root ganglia.

Although there have been many advances in the technology, relatively little has changed with the stimulation parameters until recently. In general, conventional SCS characteristics include frequency of stimulation ranging from 40 to 120 Hz, pulse duration from 0.1 to 0.3 ms, and current applied at 60–80 % of motor threshold which varies per patient. Patients vary significantly in what stimulation parameters they would like to use and the resultant perceived paresthesia they can tolerate to achieve maximal analgesia. The parameters determine energy usage by the battery and make it possible to estimate when the battery will need to be recharged. Recharging is currently done by using an external radiofrequency unit to charge the implantable pulse generator (IPG).

Relatively few clinical studies have been conducted to optimize analgesia produced via stimulation. However, basic science research helps to shape and evolve the field of SCS and allows for in-depth experimentation concerning experimentation of stimulation settings, different injury models, constant follow-up and evaluations, behavioral responses to various mechanical/thermal stimuli, and a variety of other factors that cannot readily be tested clinically. Animal models primary focus is to either better understand the electroneurophysiologic phenomena of SCS, such as through different neuronal pathways, or to better understand the mechanism of action of SCS in the hopes to make it more effective.

Most animal studies utilize a monopolar electrode while trying to maintain clinically relevant settings: typically about 50 Hz, 200 ms pulse width, and around 66 % motor threshold. It was demonstrated in animal studies that GABA upregulation in rats was observed in "responders" where no change was observed in "nonresponders" [23]. A follow-up study went on to show that the SCS-induced analgesia was reversed by adding a GABA antagonist demonstrating the significance of GABA on SCS-mediated analgesia. Many studies have also shown that the effect of SCS at subthreshold was made effective upon administration of typically non-analgesic doses of serotonin linking SCS to the serotonin pathway. Similar studies have shown that serotonin and substance P are released following SCS. Due to the link between SCS and these neurotransmitters, the efficacy of SCS with co-treatment of various neurotransmitters is summarized in Table 21.3 [27].

Table 21.3 Effect of various spinal originating transmitters on efficacy of SCS

Spinal neurotransmitter	Effect of cotreatment with SCS
Acetylcholine	Increased
Adenosine	Increased
GABA	Increased
Norepinephrine	Increased
Serotonin	Increased
Substance-P	Increased
Aspartate	Decreased
Glutamate	Decreased

Adapted from Krabbenbos et al. [27]

A clinical study was done demonstrating that tonic SCS (40 Hz) interspersed with a short 5-burst spike at 500 Hz stimulation resulted in paresthesia-free analgesia. This study supports the new stimulation protocol being tested that utilizes high-frequency stimulation to produce analgesia without the paresthesia as a side effect. The stimulation range is much higher at 10 kHz and the current averages around 4 mA. While this technique has not yet been validated, based on animal studies and a few clinical trials, high-frequency SCS may be another advancement in the field of SCS therapy. The fundamental mechanism for SCS may not be known, but as research models improve and we come to understand more of the underlying mechanism in patients responding to SCS therapy, SCS will become a more common tool for individuals suffering from chronic pain.

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New Vistas: Small-Pain-Fibers Method of Testing for Spinal Cord Assessment in Pain States

22

Alan David Kaye

Introduction

Patients present to pain clinics for a variety of problems. In fact, overall, the number one complaint in any physician office is pain. At times, the diagnosis and treatment of a given pain syndrome can be challenging. In any physical examination involving a chronic pain patient, sensory neurological examination is important. It is important to know the evolution of nerve testing and to differentiate small-pain-fibers method of testing from previous techniques. In the 1940s, a logical approach to the sensory examination was identified with defined surface areas highly correlated with specific anatomic dermatomes. These dermatomes are associated with specific nerve roots and are very useful for the clinician attempting to ascertain the source of a pain generator. The concept of current perception threshold was later developed to measure the level of sensory deficit. There was significant variability associated with this diagnostic technique, which involved changing skin resistance. These limitations led to further evolution and development of sensory conduction testing.

Sensory Nerve Conduction Threshold Testing

A sensory nerve conduction threshold test is a psychophysical assessment of both central and peripheral nerve functions. It measures the detection threshold of accurately calibrated sensory stimuli. Normal sensory nerve action potentials mean that the cells of the dorsal root ganglion and the large myelinated axons are healthy and that if a patient has numbness, the abnormal process lies proximal to the dorsal root ganglion, or the patient has common small fiber or nociceptive neuropathy. Sensory nerve conduction testing can localize the anatomic basis of the disease and may become abnormal earlier in the course of a disease state as compared with motor nerve conduction testing. This procedure is intended to evaluate and quantify function in both large and small caliber fibers for the purpose of detecting neurologic disease. Sensory perception and threshold detection are dependent on the integrity of both the peripheral sensory apparatus and peripheral-central sensory pathways. In theory, an abnormality detected by this procedure may signal dysfunction anywhere in the sensory pathway from the receptors, the sensory tracts, and the primary sensory cortex to the association

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cortex. This procedure is different and distinct from assessment of nerve conduction velocity, amplitude, and latency. It is also different from short-latency somatosensory evoked potentials. This instrument provides testing which is voltage mediated, and results are independent of changes in skin resistance. Essentially, voltage-actuated sensory nerve conduction has resulted in the development of a different type of instrument to quantitate sensory function.

Sensory nerve conduction studies are performed by electrical stimulation of a peripheral nerve and are recorded from a purely sensory portion of the nerve and the recording electrode is the more proximal of the two. Sensory latencies are on the scale of milliseconds. Sensory amplitudes are much smaller than the motor amplitudes, usually in the microvolt (μV) range. The sensory nerve conduction velocity is calculated based upon the latency and the distance between the stimulating and recording electrode.

Sensory nerve conduction information can lead to diagnosis other than peripheral neuropathy to explain the process that is occurring. It is limited in that it is not precise as to the site of deficit. This has created a need to more precisely define the specific pathological etiology.

The Small-Pain-Fibers Method

In 1998 a small-pain-fibers method was approved by the FDA. The pain-fiber nerve conduction threshold (pf-NCT) method uses an electrical stimulus with a neuroselective frequency to determine the minimum voltage causing conduction. Rather than comparing the data with population averages on a bell-shaped curve, which has about 65 % sensitivity, the patient is his own control (e.g., a nerve on the left hand is measured against a nerve on the right hand). In a 3-year Louisiana State University School of Medicine Pain Center study it was found that the nerve requiring the greatest voltage to cause conduction of the A-delta (Fast Pain) fibers identified nerve root pathology with 95 % sensitivity. The test is painless and rapidly performed. A new version uses a potentiometer to objectively measure the amplitude of the action potential applied at a distant site along the nerve being tested. The previous version required the reporting of a sensation when the nerve fired introducing potentially confounding variables. This test does not require the patient to report a sensation though one may be experienced nor does it require myelin loss to detect function change (such as nerve conduction velocity testing), so velocity is not measured.

Devices used for pf-NCT such as the PAIN-NCS and Axon-II consist of a potentiometer (detector) placed near the spine, a ground sponge placed on the back, and a test probe (stimulator) placed in close proximity to peripheral nerves being tested. An electrical stimulus of set frequency is applied with increasing amplitude until the potentiometer detects electrical nerve conduction.

In summary, the small-pain-fibers method of testing for spinal cord pathology is relatively new and largely unknown in the medical community. One such device that uses this technology is the neural scan, which has been demonstrated to serve as an effective diagnostic device designed to identify selective nerve pathology by measuring the amplitude of localized sensory nerves, not only nerve functionality. A sNCT testing device only identifies a dysfunction somewhere in a sensory pathway, making the small-pain-fibers technology valuable in terms of accuracy and precision of spinal cord pathology. A small-pain-fibers device assesses nerve pathology by measuring nerve response at differing points along a sensory nerve. It does not rely on the integrity of the overall central sensory pathways to the cortex rather specific and individual sensory nerves. Small-pain-fibers technology performs pain fiber nerve conduction studies by measuring the amplitude of the stimulus and the amplitude of the action potential. Future studies are warranted to better understand this technology and its role in identifying spinal cord pathology.

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