2 Electroencephalography and Evoked Potentials: Technical Background

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Contents

Abstract

Information provided by neurophysiological investigations is of outstanding importance for clinical practice and research dealing with patients with disorders of consciousness. However, because most of these patients are treated in the intensive care unit (ICU), some related problems must be known. The ICU is an environment full of electrical devices prone to produce artifacts, and patients with disorders of consciousness are exposed to many different treatments that may interfere with electrical signals and their interpretation. It is therefore highly important that the electroencephalogram (EEG) and the different sorts of evoked potentials (EP) are acquired under good conditions and according to current recommendations. This chapter reviews the technical background necessary to illustrate how to acquire good EEG/EP signals in the ICU, and will also focus on some practical pitfalls.

2.1 Electroencephalography (EEG)

Electroencephalography is the recording of the brain electrical activity and represents a unique way to look at the brain function in real time. This technique is very convenient for patients with disorders of consciousness in the intensive care unit: it is a noninvasive procedure that can be performed with a portable machine at bedside.

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Until the last decades of the last century, EEGs were recorded on paper. This limited the acquisition of large amounts of data and also the review of prolonged recordings. The development of digital EEG machines has completely changed the way we think about the EEG in the ICU. It is now possible to record and stock large amounts of data and also to apply complex signal analyses, such as spectral analyses and automatic seizure detection, rendering the review of prolonged records more effective. The importance of EEG evaluation has therefore increased and has become a standard in the evaluation of patients in the ICU with consciousness disorders (Kurtz et al. 2009) (see also Chap. 1). To understand how to record an EEG trace, each step between the brain EEG generators to the wave on the screen should be considered.

2.1.1 Basic Neurophysiology

The scalp EEG represents a graph of voltage differences between two different locations over time (Fisch 1999); the signal is recorded at the scalp but actually arises from pyramidal neurons located in the cortical layers, arranged in columns perpendicular to the brain's surface. The sum of thousands of synchronized postsynaptic potentials will generate electric currents recorded at the surface. The scalp EEG can only detect electrical potentials generated near the brain surface. Moreover, at least 6 cm^2 (or, roughly, one square inch) of the cortex with synchronous neuronal activity is needed to create a scalp potential (Fisch 1999). This surface activity is synchronized and modulated by complex neuronal networks involving interactions between the cortex and deep structures of the brain, mainly the thalamus, as well as other cortical areas. This will produce the rhythmicity and the waves of the brain activity seen on the EEG.

2.1.2 Impedance and Electrodes

The potentials recorded on scalp EEG are measured in microvolt (μV), typically 10–100, while, as a comparison, the electrocardiogram measures are in millivolt (mV). These voltage signals have to cross several layers and potential "electrical barriers" to reach the surface, such as the cerebrospinal fluid, the dura, the skull, and finally the scalp. Then, the current will go through electrodes and wires, which may also be considered as electrical obstacles. All these structures produce an opposition to the electric signal. In an alternating current (AC) circuit, this is called "impedance" and it is measured in Ω (Ohms). According to the International Federation of Clinical Neurophysiology (IFCN) guidelines and the American Clinical Neurophysiology Society (ACNS) recommendations, electrodes impedances should be checked before every recording and should not exceed 5,000 Ω (=5 kΩ) (Ebner et al. 1999; American Clinical Neurophysiology 2008). In practice, one can accept values up to 10 k Ω. Obtaining low and uniform impedances throughout all the electrodes is crucial in order to obtain a reliable EEG signal and avoid artifacts. On the other hand, impedances less than 1 kΩ may indicate a possible shortcut between electrodes and should be specifically addressed.

One of the major components of the impedance is the skin, particularly the outermost layer of dead cells (Eggins 1993). It is thus important to minimize this barrier by abrading the skin by applying an abrasive and conductive gel to a cotton swab and rubbing the skin before fixing the electrode. Then a conductive gel/paste should be used to assure a good contact between the scalp and the electrode. The second impedance component is the electrode itself, depending on its shape and its material.

There are many different types of electrodes available. Most contain a metal contact surface, an insulated wire, and a connecting pin. They are usually made of silver, gold, tin, or platinum and coated with chloride-treated silver. There is an important issue regarding metal electrodes and brain imaging, which is often required in critically ill patients: metal electrodes have to be removed because they can cause important artifacts. Moreover, while there is no safety issue with CT scan, classical electrodes may warm and cause scalp burns during MRI studies. Some newer electrodes are MRI and CT compatible and are made of con-

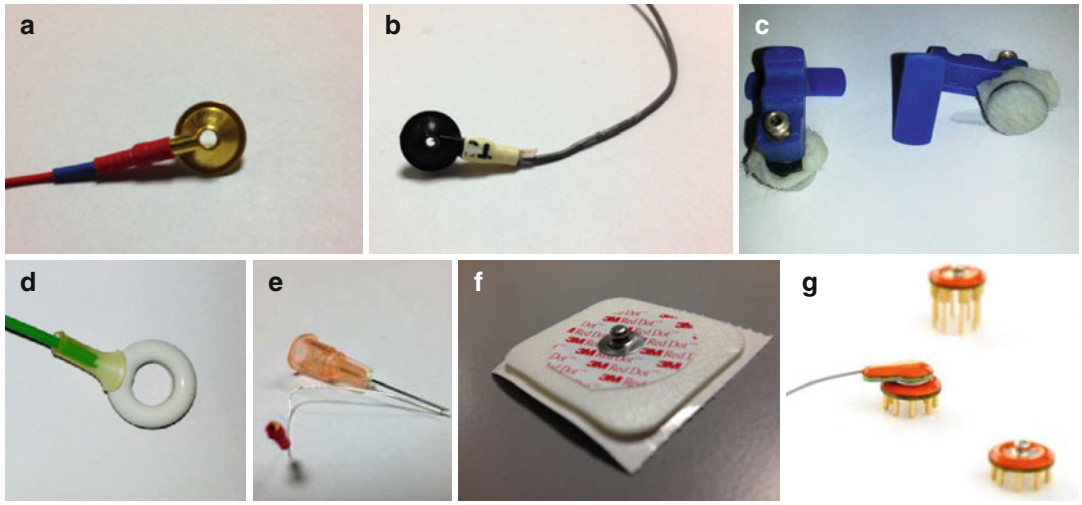

Fig. 2.1 Different types of electrodes. (**a**) Gold cup electrode. (**b**) Plastic cup electrode CT/MRI compatible. (**c**) Pad electrode. (**d**) Ring electrode. (**e**) Subdermal electrode (also available as MRI/CT compatible). (**f**) Auto-adhesive, pre-gelled, disposable electrode. (**g**) Dry electrode (g.SAHARA®, G-tec medical engineer, reprinted with kind permission)

ductive plastic with a thin silver coat, coupled with very short leads (Das et al. 2009). These conductive plastic electrodes, increasingly in view of their practical advantages, enable good quality EEG recording with no CT artifacts and only minor MRI changes, without any safety issues. Of note, this kind of system may need to be removed if a conventional arteriography is needed, as the projection of the electrodes and wires will impact on the interpretation of this investigation.

There are several different types/shapes of electrodes that can be used in the ICU (Fig. 2.1):

- *Cup electrodes* have typically a diameter of 4–10 mm and a hole on its top to allow the application of saline gel (for conduction), as on a typical EEG. For monitoring, these have to be fixed on the scalp with an adhesive plaster (Fig. 2.1a). Of note, after 10–14 days of recording, 2–3 days without electrodes ("electrode holiday") are advisable to prevent skin damages. These electrodes are recommended by the IFCN for EEG monitoring (Chatrian et al. 1996). CT-/MRI-compatible plastic cup electrodes are also available (Fig. 2.1b).
- *Pad electrodes* held in place with a rubber headset are convenient because they allow a precise placement even in patients with small skull defects or skin scars and avoid the fastidious work of standard cup electrodes fixation/removal. However, they are neither suitable for EEG monitoring, nor for patients with significant skull defects (Fig. 2.1c).
- *Ring electrodes* fixed with electrode holder on a textile cap allow a rapid placement (Fig. 2.1d). Moreover, commercially available caps are built according to the international 10–20 system (see below). However, these are not suitable for patients with skull defects or recent skin scars and do not assure a satisfying long-term contact for EEG monitoring. This type is also prone to shortcuts between different electrodes, because of the important amount of conductive gel needed.
- *Subdermal electrodes* made of stainless or platinum needles (Fig. 2.1e). Because these are placed under the epidermis, skin abrasion is not necessary. They can be applied very quickly; however, because of their small diameters, they may have a relatively high impedance (Freye E & Levy J. 2005) even though they penetrate the skin. Because of their subdermal position, they are only suitable for comatose patients and may induce local skin infection.
- *Disposable and pre-gelled pad electrodes* (Fig. 2.1f). These could possibly decrease the risk of cross-contamination inherent to stan-

dard electrodes and spare time to the technician team by eliminating the time required for disinfection. These electrodes are however difficult to use over the hair.

- *Dry electrodes* (Fig. 2.1g). This new type of electrodes is now commercially available but not routinely used in clinical practice. Their name is due to the fact that neither gel nor skin preparation is needed. In view of their quick application and good impedance, this type of electrodes may be more frequently used in the future.

Every electrode type has thus its advantages and disadvantages summarized in Table 2.1, but cup electrodes fixed on patient's scalp with an adhesive conductive paste, represent probably the most suitable type for EEG monitoring.

2.1.3 Electrode Position and Montages

2.1.3.1 Electrode Position: The 10–20 System

The IFCN proposes a unified electrode nomenclature and electrode placement, called the 10–20 system (Klem et al. 1999), which includes 21 electrodes providing a good scalp coverage. This international and widely adopted system should be used on every scalp EEG in the ICU. The electrodes are named with a letter, representing the anatomical region (Fp = frontopolar, F = frontal, C = central, P = parietal, T = temporal, and O = occipital), and a number (even numbers on the right and odd numbers on the left; midline electrode is called z (zero)) (Fig. 2.2). The

Table 2.1 Pros and cons for every type of EEG electrode

Electrode type	Pros	Cons
Cup electrodes	Good impedance	Time consuming
	Can be used for long-term monitoring	Technician needed
	Possible electrode placement modification if required (skull defects, skin scar, clip, etc.)	
	Recommended by the IFCN	
	CT-/MRI-compatible electrodes available	
Pad electrodes	Good impedance	Only some hours of good recording
	Relatively fast setup	Not suitable for patient with significant skull defect
	May be used on patients with minor skull defect	Technician most often needed
	Possible electrode placement modification if required (skin scar, clip, etc.)	
Ring electrodes	Good impedance	Only some hours of good recording
	Fast setup	Prone to bridge because of the important quantity of conductive paste needed
		Not suitable for patients with skull defects
		Electrode placement modification is impossible
		Technician most often needed
Needle electrodes	Fast setup	Only suitable for comatose patients. May have a relatively high impedance because of small diameter
	CT-/MRI-compatible electrodes available	Technician/nurse most often needed
		May be prone to skin infection
Disposable and pre-gelled electrodes	Fast setup	Difficult to use over hair, so full scalp coverage is impossible
	No risk of cross-contamination	Fair impedance
	Can be placed by any healthcare provider with minimal teaching	
Dry electrodes	Good impedance	Cost
	Fast setup because no skin preparation is needed	Mostly used for current research
		Not widely used in clinical practice

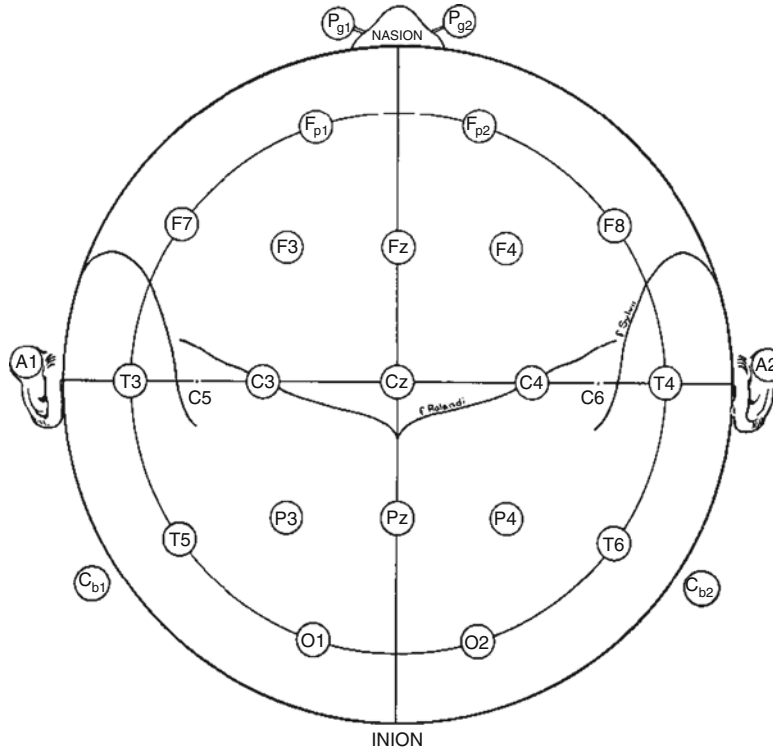

Fig. 2.2 A single plane projection of the head, showing all standard positions according to the 10–20 system (Adapted from Klem et al. (1999). © International Federation of Clinical Neurophysiology. Reprinted with kind permission from the International Federation of Clinical Neurophysiology)

system is called 10–20 because each electrode is separated with 10 or 20 % of an anatomical distance.

The guidelines edited by the IFCN provide detailed methods of the electrode placement based on anatomical landmarks (Klem et al. 1999). The first step is to place the midline chain of electrodes, Fpz, Fz, Cz, Pz, and Oz (Fig. 2.3), by measuring the distance between the nasion and the inion through the vertex. Of note, Fpz and Oz positions will not be covered by an electrode. The next step is to measure the coronal distance from the left preauricular point to the right one through Cz. This will provide the position of T3 (also named T7), C3, C4, and T4 (also named T8) (Fig. 2.4). Then, in order to obtain the position of Fp1, F7, T5 (also named P7), and O1 on the left and Fp2, F8, T6 (also called P8), and O2 on the right, a circumferential measurement of the head through Fz, T3, Oz, and T4 should be obtained (Fig. 2.5). Finally, F3 should be placed at the intersection of Fp1–C3 and F7–Fz, F4 at the intersection between Fp2–C4 and Fz–F8, P3 at the intersection of C3–O1 and Pz–T5, and P4 at the intersection between C4–O2 and Pz–T6. A cerebral or extracerebral reference electrode, a ground, and an electrocardiogram should be placed eventually.

2.1.3.2 Montages

The types of montages are highly variable in every center. The same montages used for routine EEG should be used. Some bipolar and referential arrangements are proposed by the ACNS (American Clinical Neurophysiology 2006a) and can be easily applied. Of note, the most popular is the traditional longitudinal bipolar montage (also known as "the double banana") (Fig. 2.6). The use of the 21 electrodes provided by the 10–20 system offers good scalp coverage, but, in selected cases, montages with fewer electrodes can be used. To determine brain death, for example (this only applies in certain countries), the distance between electrodes should be at least 10 cm. The ACNS recommends a bipolar montage using 10 electrodes, for example, F7-T5, F8-T6, F3-P3, F4-P4, and Fz-Pz (American Clinical Neurophysiology 2006b).

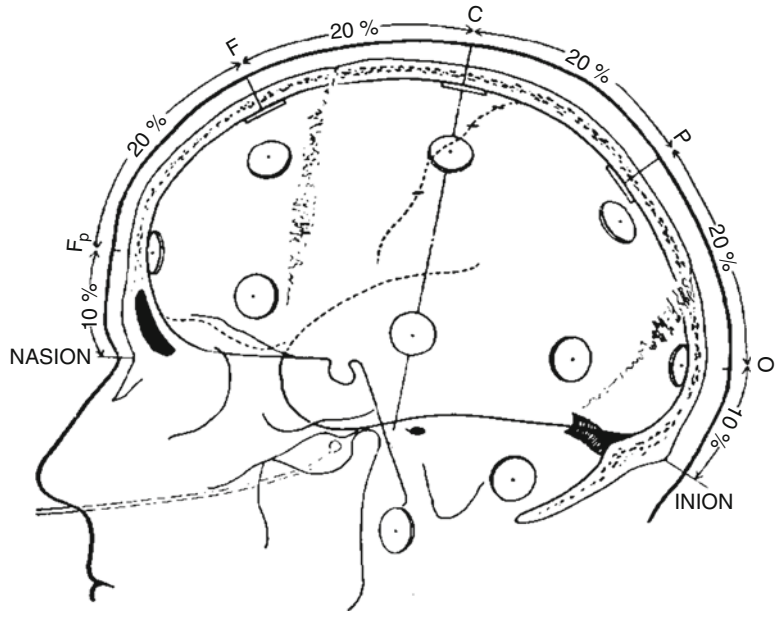

Fig. 2.3 Lateral view of the skull to show methods of measurement from nasion to inion at the midline. Percentages indicated represent proportions of the measured distance from the nasion to the inion (Adapted from Klem et al. (1999). © International Federation of Clinical Neurophysiology. Reprinted with kind permission from the International Federation of Clinical Neurophysiology)

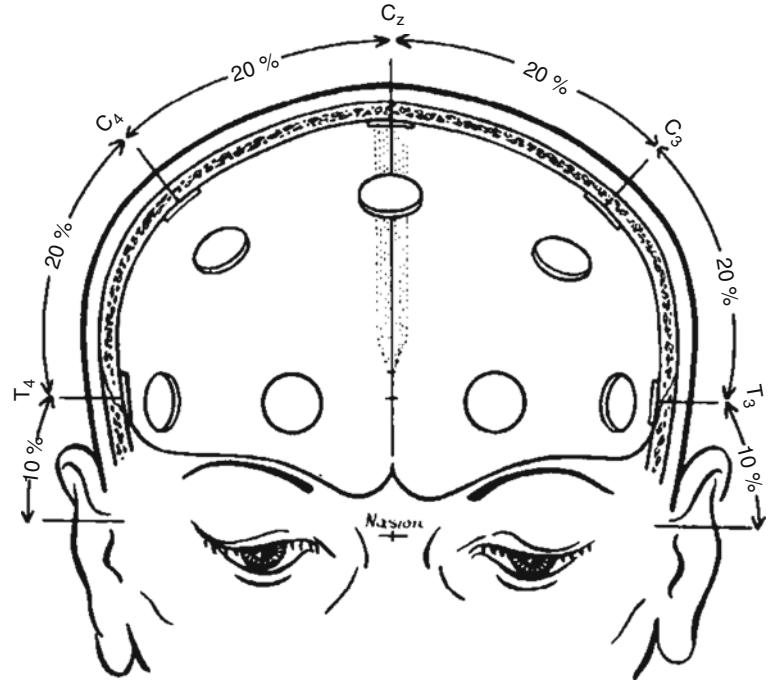

Fig. 2.4 Frontal view of the skull showing the method of measurement for the central line of electrodes as described in the text (Adapted from Klem et al. (1999). © International Federation of Clinical Neurophysiology. Reprinted with kind permission from the International Federation of Clinical Neurophysiology)

2.1.3.3 Other Montages/Electrode Positions

Anterior Temporal Electrodes

If the temporal regions are an important issue, two additional electrodes can be added to maximize the anterior temporal lobe coverage. These are called T1 (left) and T2 (right). They are placed one cm above the line cut at the third next to the ear, between the external angle of the eye and the preauricular point.

Extracerebral Electrodes ("Polygraphic Recording")

Additional electrodes placed near the eyes (to record eye movements), on selected muscles (to record particular body region of interest, such as

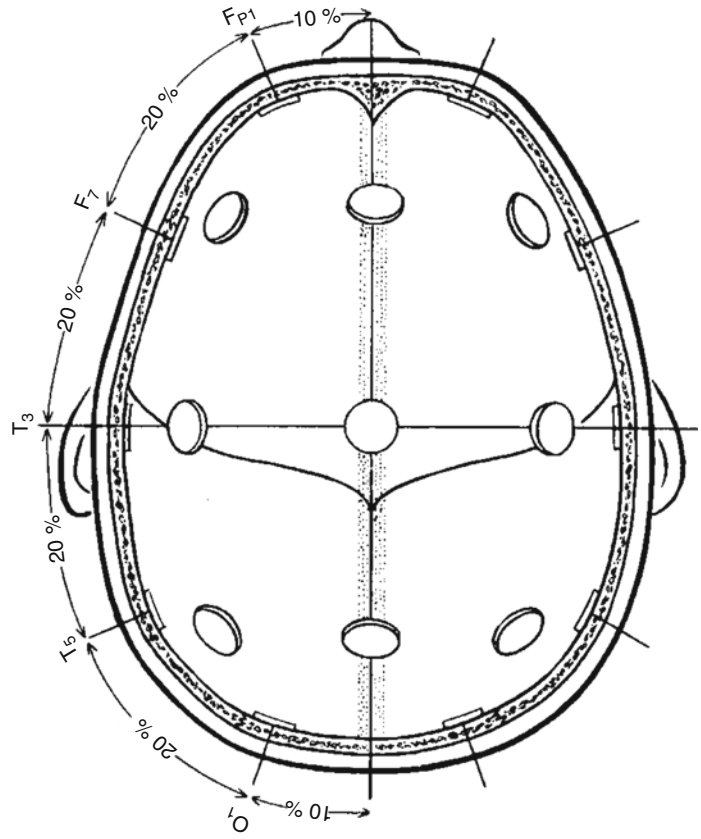

Fig. 2.5 Superior view with cross section of the skull through the temporal line of electrodes (Adapted from Klem et al. (1999). © International Federation of Clinical Neurophysiology. Reprinted with kind permission from the International Federation of Clinical Neurophysiology)

the tibial and the submental regions) and respiratory electrodes (measuring the movements of chest and abdomen) can also be added. These additional electrodes can be helpful to discriminate between cerebral or extracerebral activities and artifacts. A routine extracerebral electrode (pair) is the EKG.

"Subhairline" Montages

Because most of the centers cannot provide 24/7 EEG technician coverage, some simple montages that can be placed with auto-adhesive electrodes have been developed. To avoid scalp and hair issue, disposable and pre-gelled pad electrodes are placed just below the hairline. Of note, EKG electrodes can be used for this purpose. A study demonstrated a sensitivity of only 68 % but a 98 % specificity for seizure detection using a 4-channel commercial ICU bedside monitoring system (Young et al. 2009) (Fig. 2.7). Another study retrospectively recreated a digital "subhairline" EEG from standard 10–20 EEG by

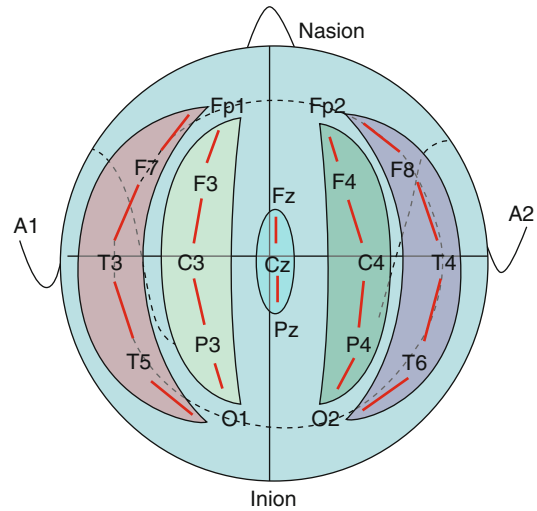

Fig. 2.6 The longitudinal bipolar or the "double banana" montage

using only 8 electrodes: Fp1, F7, T3, and T5 on the left and Fp2, F8, T4, and T6 on the right. The sensitivity for seizure detection was only 72 % (Kolls and Husain 2007). The addition of

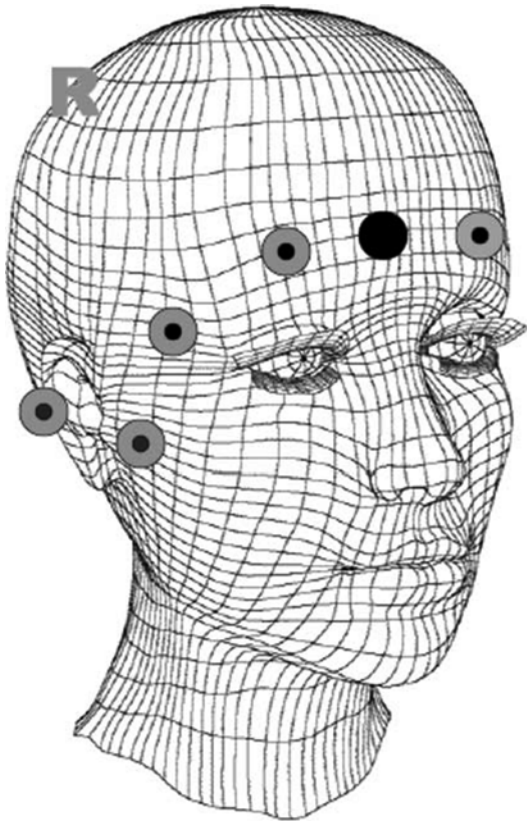

Fig. 2.7 Example of a "subhairline montage" (Adapted from Young et al. (2009), Figure 1, ©Humana Press Inc. Reprinted with kind permission from Springer Science + Business Media B.V.)

Fig. 2.8 Example of a disposable auto-adhesive EEG device (StatNet™, HydroDot Inc., reprinted with kind permission)

Cz seems to increase the sensitivity up to 92 % (Karakis et al. 2010).

Disposable Devices

Some disposable and quickly applicable "electrode systems" have been developed. For example, pre-gelled EEG headpieces, embedded with integrated wiring, are commercially available (Fig. 2.8). However, these only provide about 4 h of reliable recording with usually less than 21 scalp electrodes; they cannot be used on patients with skull defect, and, because of the disposable nature, related costs should be considered. It seems reasonable to consider this system when a standard electrode placement is not available and the EEG information is needed immediately.

2.1.4 Jackbox, Amplifiers, and Filters

2.1.4.1 Jackbox

Each electrode's wire will be plugged in a jackbox (Fig. 2.9). Many devices often surround the ICU beds; therefore, a small jackbox that can be placed near the patient's head is recommended. The jackbox should also be fixed and possibly sealed into a waterproof packing to avoid damage (Herman 2013). The jackbox contains the amplifiers; according to the IFCN (Ebner et al. 1999), at least 23 connectors (amplifiers) are required for clinical practice. However, larger capacity input systems are available (for higher special resolution and extracerebral electrodes).

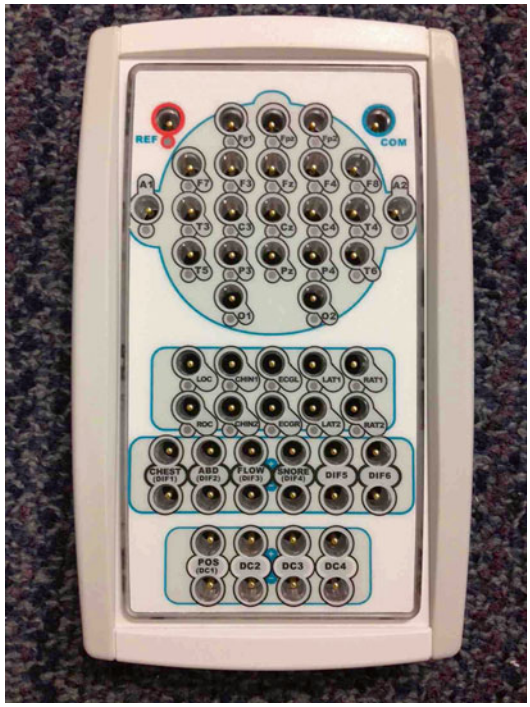

Fig. 2.9 An example of an EEG jackbox

2.1.4.2 Amplifiers

EEG amplifiers have two functions: discrimination and amplification (Fisch 1999). Discrimination is the ability to amplify the difference between two electrical potentials: the amplifier will subtract the signal of two different input EEG electrodes, between two adjacent scalp electrodes on a bipolar montage or between one electrode and a common reference for a referential montage, for example. Of note, the subtraction implies that signals common to both subtracted electrodes will be suppressed (this may also give rise to the "electrical bridge," when an analogous signal between two electrodes is seen as a flat line in a bipolar montage). Artifacts that are common to both electrodes will also be suppressed. In this way, an amplifier can sort out true EEG brain signals and artifacts. This discrimination power can be measured with the "common mode rejection ratio": the higher this ratio, the higher the discrimination power. With current EEG machines, the specified common mode rejection ratio should be at least >80 dB, typically 100 dB (Ebner et al. 1999). Then, the amplifier will increase the potential difference; this effect is called "gain" or sensitivity. A typical setting for EEG is 7–10 uV/mm.

2.1.4.3 Filters

Filters are used to exclude frequencies that are not generated by the brain. In clinical practice, frequencies of interest are between 1 and 30 Hz. Therefore, the low-frequency filter (synonymous with high-pass filter) should be set at 0.5–1 Hz and the high-frequency filter (or low-pass filter) at 70 Hz. A notch filter of 50 or 60 Hz (depending on the country) for power line artifacts should be used when needed. Of note, it is advisable to start the recording without the notch filter, as electrodes with loose contact to the scalp will tend to show a prominent notch artifact.

2.1.5 Digital EEG and Video

Nowadays, nearly all EEG recordings are digital. While the advantages are obvious, this implies some precautions.

2.1.5.1 Digitalization: Sampling Rate and Resolution

To be recorded on a computer, a wave has to be sampled. According to the Nyquist theorem, the sampling rate of a sinusoidal wave should be at least two times higher than the recorded frequency. However, this represents the strict minimum requirement, and to avoid aliasing effects (Fig. 2.10), the sampling rate should be at least 3 times the high-filter setting (American Clinical Neurophysiology 2006c). Since the high-frequency filter is typically set at 70 Hz, a 250 Hz sampling rate is reasonable for clinical purposes. Higher sampling rates may be used, but will produce much larger file sizes. Since recordings should be able to resolve EEG down to 0.5 uV, digitization should use a resolution of 12 or more bits (American Clinical Neurophysiology 2006c).

2.1.5.2 Screen

EEG traces should be read on working stations equipped with screens larger than 17", allowing a comfortable analysis. Multiple screens could even

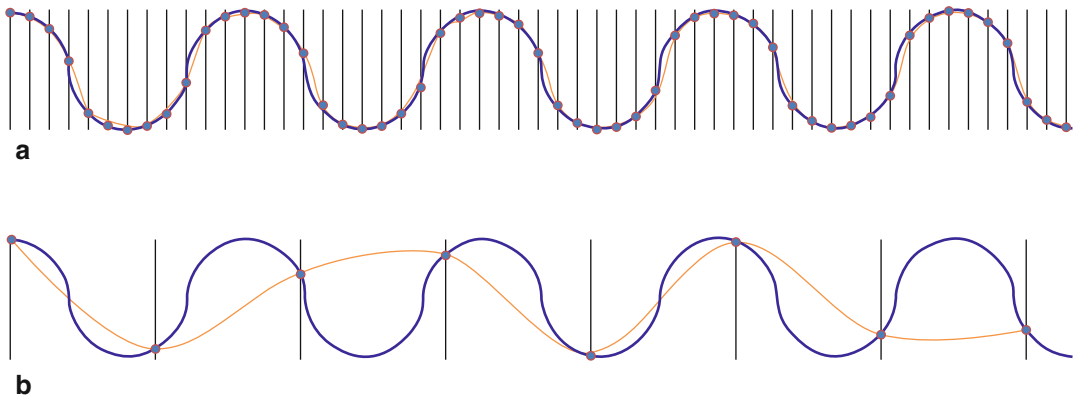

Fig. 2.10 Sampling rate and aliasing effect. In *blue*, original sinusoidal wave; in *orange*, digitalized sinusoidal wave; in *black*, sampling rate. (**a**) Due to appropriate sampling rate, the digital sinusoidal wave matches the original one. (**b**) Due to insufficient sampling rate, the digital wave looks too slow = aliasing effect

be better, especially if additional signals have to be evaluated (such as quantitative EEG analysis).

2.1.5.3 EEG Software and Network

Every EEG system has its own EEG software, featuring the basic requirements needed for a standard analysis. A complementary software providing spectral analysis, automatic seizure detection, symmetry index, and other features is advised for ICU monitoring. Indeed, these tools render the analysis of prolonged EEGs more efficient and may save considerable time (Moura LMVR et al. 2014). The software used on the recording machine should be user-friendly enough for inexperienced EEG healthcare providers, in order to easily add annotations on EEG trace. In the same setting, a "push-button" possibility (to mark an event of clinical significance) should be offered. Because ICU EEG should be interpreted at any time, an acquisition machine should be ideally plugged on a network and be accessible anytime from the working/reading station.

2.1.5.4 Data Storage

Data storage also represents an important issue. Prolonged continuous EEG recordings generate large amounts of information to be saved. The storage of the entire EEG traces and only the pertinent video part represents a good compromise. There is no consensus for the best data backup (CD, DVD, hard drive, secured network, etc.). While the latter seems to offer the best security, specifically advantages and disadvantages have to be weighed with each hospital informatics team and availabilities.

2.1.5.5 Video

Video recording is strongly recommended on every ICU monitoring. Many artifacts cannot be identified without a correlated video. Moreover, electro-clinical correlation can be carefully analyzed in case of seizures, for example. A wide-angle high-resolution camera is recommended. The zoom should set in a way that at least the face and the arms of the patients are seen. Because EEG machines are frequently moved, the framing should be checked and corrected regularly.

2.1.6 The EEG at the Bedside: Practical Aspects in the ICU

There are some highly relevant practical issues specific to the ICU to be considered before every EEG recording. Patients in the ICU are exposed to many external factors that can influence the EEG trace and thus its interpretation.

2.1.6.1 Body Temperature

It is known that even without brain pathology, hypothermia leads to progressive EEG slowing and finally EEG suppression (Mezrow et al. 1994), but without important clinical issue until a temperature under 30 °C. Indeed, in a series of 47 patients undergoing profound hypothermia for aortic surgery, the EEG first showed periodic complexes over a continuous background at a mean temperature of 29.4 °C (±3 °C), a burst-suppression pattern appeared at 24.4 °C (±4 °C), followed by a complete EEG silence at a 17.8 °C

(±4 °C) (Stecker et al. 2001). EEG can be recorded during mild therapeutic hypothermia to 32°–33 °C, after brain anoxia, for example (Rossetti et al. 2012), but this should be considered during interpretation, as the temperature and the related pharmacological sedation (this aspect seems to have more weight) may mildly slow and reduce the amplitude of the signals.

2.1.6.2 Medication

Sedative drugs, antipsychotic drugs, antiepileptic agents, and all compounds with an effect on the central nervous system could potentially alter the EEG trace. Patients in the ICU are particularly exposed to these drugs. All medication should be listed and known.

2.1.6.3 Skull Defect

A skull defect, as small as a burr hole or as big as a large craniotomy, can cause a "breach rhythm" (focal accentuation of fast activity) and can be misleading if unknown. There is no clear correlation between the size of the skull defect and the importance of the breach rhythm.

2.1.6.4 Muscular Activity

Unresponsive patients may present a variety of involuntary movements, like myoclonus or shivering, which can produce significant artifacts. If the EEG monitoring is non-interpretable because of movement artifacts, a transitory muscular blockade can be considered (Chatrian et al. 1996). Short-acting agents are preferred, such as vecuronium or succinylcholine. Only trained healthcare providers should administer these drugs; it is common practice to add some mild sedation at the same time; this should not impact the global architecture of the recordings.

2.1.6.5 Electrical Devices

Electrical interference can result from numerous sources in the ICU, in view of the high technical support needed to treat these patients. In case of any non-concordant findings on the curves, these devices have to be considered as an artifact generator, for example, mechanical ventilator, external cardiac support, dialysis devices, electric bed, anti-scar mattress, or perfusion pumps.

2.1.6.6 Reactivity Assessment (See Also Chap. 5)

Reactivity should be assessed for every EEG performed on patients with impaired consciousness, unless there is a concern of raised intracranial pressure due to stimuli (Young 2000). EEG background reactivity is associated with a potential of recovery (Young et al. 1999), particularly in the context of brain anoxia (Rossetti et al. 2010). Timing of each stimulus has to be clearly noted on the EEG trace. Auditory stimuli (loud calling, hand clapping far from the electrodes) should be started first. Eye opening (under a light source) may be applied next. Then, noxious stimuli will be tested. Painful stimuli over the trunk are preferred. Indeed, temperature, focal compressive neuropathies, spinal cord lesions, and stroke can all make noxious stimuli applied on the limbs less reliable, while axial regions are mostly bilaterally represented in the brain. Sternal rubbing, pressure on the supraorbital nerve above the eyebrow, and mandibular advancement will produce EEG artifacts. We recommend nipple pinching, as it provides a strong noxious stimulus without inducing artifacts. We also recommend not performing stimulations less than 20" apart, in order to allow the patient (and the EEG) to recover to baseline.

2.1.6.7 Length of EEG: LTM or Spot EEGs? (See Also Chap. 5)

This major question is still unsolved, and the IFCN recommendations do not address it (Guérit et al. 1999). EEG monitoring is highly "resource consuming"; on the other hand, a continuous EEG undoubtedly appears attractive and allows the follow-up of the evolution of the patient's brain activity. It has recently been shown that two standard intermittent EEGs (20–30 min) show a comparable performance than continuous EEG for outcome prognostication and identification of epileptiform transients in a relatively small sample of comatose survivors of cardiac arrest (Alvarez et al. 2013). On the other hand, EEG monitoring detects more seizures (which are frequently non-convulsive) (Claassen et al. 2004) and has repetitively proven to be important for the management of comatose patients with subarachnoid hemorrhage (Lindgren et al. 2012),

intracerebral hemorrhage (Claassen et al. 2007), or traumatic brain injury. A recent retrospective study focusing on mechanically ventilated patients shows an association between the use of continuous EEG monitoring and a lower mortality rate (Ney et al. 2013). Overall, the recording length should be discussed for each case, based on the clinical setting and EEG availability on a daily basis.

2.2 Evoked Potentials

Evoked potentials (EPs) correspond to EEG alterations in response to a stimulus (Guérit 2005). The stimulus can be somatosensory (somatosensory evoked potential) (SSEP), auditory (auditory evoked potential (AED), or visual (visual evoked potential (VEP). There are different types of EPs, depending on the timing of recording: "short-latency" evoked potentials correspond to the recordings of signals generated by the ascending pathways and the primary cortex; "middle" or "long" latency potentials represent more complex waves reflecting brain network activities, such as "cognitive" potentials. In routine clinical practice, short-latency EPs are the most widely used. The main advantage of the EP technique is that it reflects the function of certain neuronal pathways, thus complementing structural information given by imaging studies; EPs are also relatively resistant to even consequent doses of pharmacological sedation, as opposed to the EEG. Moreover, EPs give numeric data that may prove useful for follow-up. In the ICU practice, SSEPs are widely used and AEPs far less frequently. Because VEPs require patient's attention for good signals, they are rarely, if at all, used in this setting and thus will not be discussed further.

2.2.1 General Considerations

EPs are, like EEG, recorded at bedside: the same practical considerations regarding artifacts as described above have to be kept in mind. Of note, EPs are generally highly "resistant" to sedation or hypothermia. Cortical somatosensory evoked potentials remain present even at a sedation level sufficient to induce an isoelectric EEG (Cruccu et al. 2008), albeit with some prolonged latency and reduced amplitude. Whereas EEG signals may disappear with body temperature under 24 °C, cortical somatosensory evoked potentials remain present until 21 °C and AEPs disappear only under 20 °C (Cruccu et al. 2008). These temperature cutoffs are usually not reached in clinical practice, even with therapeutic hypothermia. However, EP signal amplitude is much smaller than EEG, thus requiring multiple trial averaging. The number of trials depends on the type of EP.

The naming of the EP signal is quite intuitive. All are made up of one letter and a number: the letter *P* or *N* represents the wave polarity (*P* for positive and *N* for negative) and the number the delay (in ms) between the stimulation and the wave. For example, the main cortical wave obtained after median nerve stimulation is negative and appears at around 20 ms after the electrical stimulation; it is thus called N20.

2.2.2 Somatosensory Evoked Potential (SSEP) (See Also Chap. 6)

These represent the electrophysiological response to the stimulation of the sensory pathways (dorsal column–lemniscal system). SSEPs can be elicited from every nerve, although the median and the tibial nerves are the most widely used and recommended by the IFCN (Maugnière et al. 1999). In patients with consciousness disorders, SSEP assessment is frequently limited to the median nerve (Chatrian et al. 1996). Therefore, only the median nerve EP stimulation will be described.

2.2.2.1 Stimulation

SSEPs are usually obtained with bipolar electrical transcutaneous nerve stimulation. The IFCN recommendations are to use monophasic square electrical pulses of 100–500 μs with two electrodes (Maugnière et al. 1999). The anode (the positive electrode) should be placed on the wrist crease and the cathode (the negative

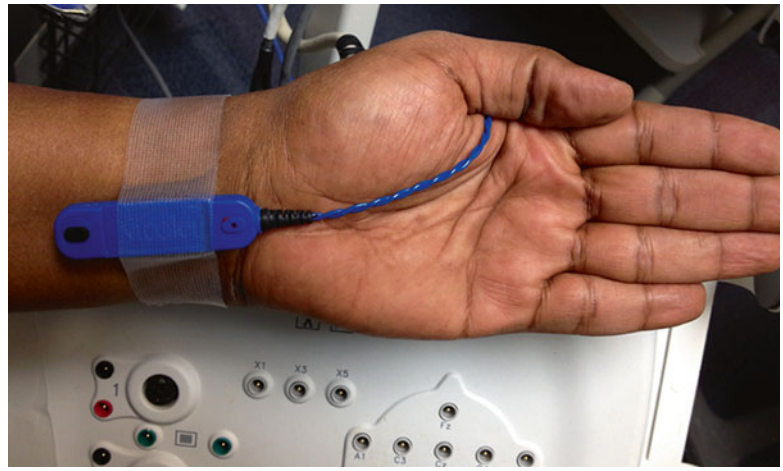

Fig. 2.11 An example of median nerve stimulation for SSEP: The anode (the positive electrode) is placed on the wrist crease and the cathode should be 2 cm proximally

electrode) should be 2 cm proximally (Fig. 2.11). The contraction of the thenar muscles can be used as an indicator of the correct location of stimulation. Both sides should be sequentially tested. The intensity of the signal should be just above the motor threshold. A stimulus rate of 3–5 Hz is recommended for routine practice (Cruccu et al. 2008); at least 500 trials should be averaged.

2.2.2.2 Recording

EEG disk electrodes should be used for recording with impedance lower than 5 kΩ. The filters should be set at 3 Hz for the low-frequency filters and 2,000 Hz for the high-frequency filters (Maugnière et al. 1999). In general, SSEPs are recorded at three levels: the peripheral, spinal cord, and cortex (Misulis and Fakhoury 2001a).

- A peripheral electrode is placed over the Erb's point ipsilateral to the stimulation (within the angle formed by the posterior border of the clavicular head of the sternocleidomastoid muscle and the clavicle, 2–3 cm above the clavicle). It is called *EPi* (for Erb's point ipsilateral).
- A spinal electrode is placed over C5 (or C6) spinous process. It is called *C5s*.
- Two cerebral electrodes are used: one ipsilateral (called *CPi*) to the stimulus and one contralateral (called *CPc*). These are placed halfway between C3 and P3 on the left (and labeled P3') and between C4 and P4 on the right (P4').
- A reference electrode (*Ref*) should be placed over the distal arm or the ipsilateral ear or over the Fz position, for example. A non-cephalic reference may provide more informative recordings but is technically more difficult (Cruccu et al. 2008).

The SSEP montage includes four channels:

- Channel 1: CPc–CPi (optional)
- Channel 2: CPc–Ref
- Channel 3: C5s–Ref
- Channel 4: EPi–Ref

Of note, some authors recommend a channel CPi–Ref (Misulis and Fakhoury 2001a) (see also Chap. 6). This channel is useful to record some deeper potentials called "far-field potentials." It does not provide any further information for outcome prediction in comatose patient in the acute setting. Thus, it is not recommended to perform it routinely in this setting.

2.2.2.3 Wave Names

Four waves are of particular interest in median nerve SSEPs in critically ill patients (Fig. 2.12):

- *N9*: It is recorded at Erb's point. N9 is particularly important because its presence assures that stimulation is effective and that the peripheral sensory system is functioning. An SSEP cannot be interpreted if N9 is not present.
- *N13*: It is recorded over the spinal electrodes and thus represents the potential generated by the dorsal horn neuron in the cervical medulla. As for N9, if N13 is not present, cortical SSEP should not be interpreted.

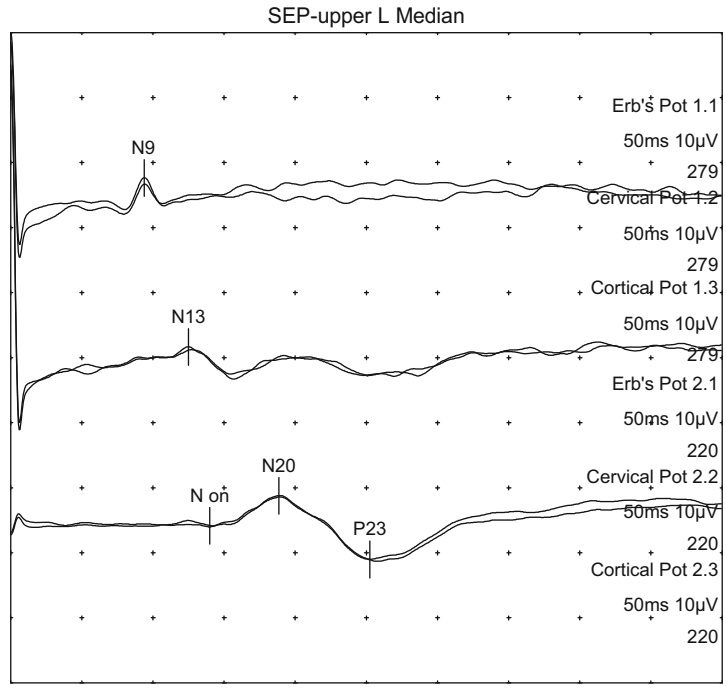

Fig. 2.12 Example of a normal SSEP obtained from median nerve stimulation. The *first line* represents the reference-Erb's point channel and displays N9. The *second line* represents the reference-cervical channel and displays N13, and the *bottom line* represents the reference-cerebral contralateral and displays N20 and P23

- *N20*: It is recorded over the parietal region and is generated by thalamocortical projections. Of note, although the negative (upward) N20 is the wave used for clinical interpretation, a small amplitude response can be identified thanks to the following positive (downward) wave; the latter should always be recognizable (see below).
- *P23*: N20 is usually followed by a positive deflection occurring 23 milliseconds after the stimulus.

Following parameters are important and should be described: the wave presence or not, the amplitude, and the latency.

2.2.3 Auditory Evoked Potential (AEP)

These represent the auditory pathway response to an auditory signal. The short-latency AEPs provide information about generators located between the acoustic nerve and the mesencephalon and thus allow a functional evaluation of the brainstem. For that reason, short-latency AEPs are frequently called the brainstem evoked potentials (BAEPs). These may be useful in cerebral death evaluation (in some countries), to assess brainstem dysfunction or to identify coma etiology when used in conjunction with other EPs (Chatrian et al. 1996). Middle- and long-latency auditory evoked potential are less frequently used in patients with consciousness disorders; these are "cognitive" potentials, and especially the "mismatch negativity" or the P300 may be of help for assessing prognosis in selected comatose patients (Tzovara et al. 2013). This topic is covered in Chap. 7.

2.2.3.1 Stimulation

Headphones or earplugs should be used to deliver a sound to the ear. Sounds consist usually of square wave "clicks," which should have these specificities (Misulis and Fakhoury 2001b):

- Stimulus duration, 100 µs.
- Stimulus rate, 8–10 Hz.
- Stimulus intensity: typically 70 dB in ICU (Freye 2005). The contralateral ear is "masked" with a white noise of 40 dB below the click level.
- While averaging 500 trials is enough for SSEP, BAEP should be based on 2,000 stimulations.

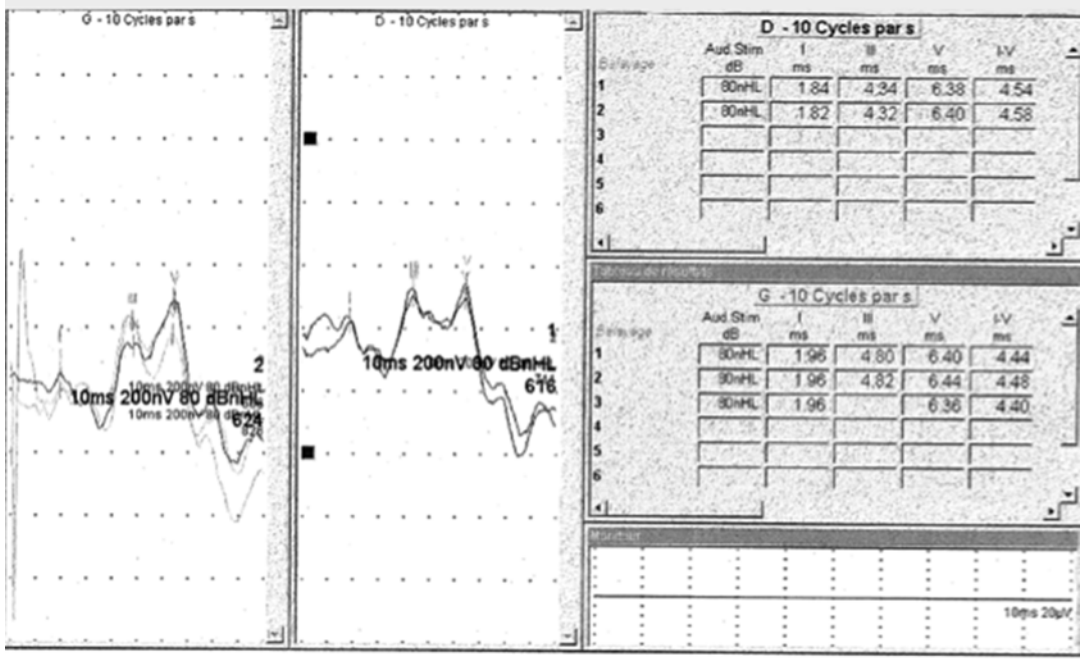

Fig. 2.13 An example of normal contralateral and ipsilateral brainstem auditory evoked potentials. Stimulation: 10 Hz at 80 dB. Wave latencies and I–V intervals are displayed on the right

2.2.3.2 Recording

- The filters should be set at 10–30 Hz for the low-frequency filters and at 2,500–3,000 Hz for the high-frequency filters:
- Four electrodes should be placed (Misulis and Fakhoury 2001b):
- One near each ear (e.g., ear lobe or over the mastoid), called *A1* and *A2*
- One over vertex on the scalp, called *Cz*
- And finally a ground at Fz or elsewhere over the head or the body

The BAEP montage includes 2 channels:

- Cz–A1
- Cz–A2

2.2.3.3 Wave Names

Five waves are described in BAEPs (Israel et al. 1999) (Fig. 2.13):

- *Wave I*: It is the first wave seen with ipsilateral ear stimulation and represents the acoustic nerve signal near the cochlea.
- *Wave II*: It is usually less consistent than Waves I and III (see below) and may be absent in normal subjects. It is thought to be generated by the proximal acoustic nerve near the cochlear nucleus.
- *Wave III*: It is usually one of the most prominent waves and probably generated by auditory pathways in the lower pons (including the upper olives).
- *Waves IV and V*: These waves are usually part of the same complex and are probably generated by the lateral lemniscus in the higher pons and the inferior colliculus in the caudal mesencephalon.

Several inter-wave distances are assessed. These are age dependent (especially in children). Normal values should be known for every BAEP laboratory according to the age of the subject:

- *I–V interpeak interval:* It represents the global response from the distal acoustic nerve to the midbrain. Its typical length is 4.5 ms.
- *I–III interpeak interval*: This interval reflects the conduction between the acoustic nerve and the pons. Its typical length is 2–2.5 ms.
- *III–V interpeak interval*: It correlates with the brainstem conduction time from the pons to the midbrain. Its typical time is 2–2.5 ms.

The presence of each wave is also of particular importance. If all waves are absent, a technical problem should be actively ruled out. A complete absence of response can however happen in severe hearing loss, acoustic nerve dysfunction, or brain death.

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