Intraoperative Somatosensory and Motor Evoked Potential Recording and Electroencephalographic Monitoring Usefulness During Aneurysm Surgery

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Abstract: In the last 20 years, there have been advances in techniques and instrumentation for intracranial aneurysm exposure and obliteration [94]. However, it seems that 32% of the patients, who underwent surgery, suffer a fatal outcome or some form of sequelae [20]. Primary brain damage due to subarachnoid haemorrhage (SAH) and to a vasospasm, is the major cause of mortality and morbidity; but surgery-related complications constitute 14% of the morbidity [20]. Indeed, the surgical therapy of cerebral aneurysms carries several risks related to manipulation, accidental or intentional blood vessels clipping, or bleeding due to premature aneurysm rupture, suggesting room for improvement in surgical procedures.

Today, electrophysiological monitoring with somatosensory and motor evoked potential (SSEP and MEP) recording, and electroencephalographic (EEG) monitoring, are frequently used in aneurysm surgery, and they are the standard techniques used in level assessing of cerebroprotective anaesthesia and monitoring ischemia during surgical manoeuvres.

In this chapter, we report our experience in using neurophysiopathological monitoring during aneurysm surgery with particular reference at the evoked potential and EEG changes in response to surgical and anaesthetic variables; we also give technical advice and discuss clinical applications. However, to prove intraoperative usefulness, these techniques requires a dedicated knowledge, both technical and pathophysiological.

Keywords: Electrophysiological monitoring, aneurysm surgery, electroencephalographic monitoring, somatosensory evoked potential, motor evoked potential, anesthetic drugs, TCI.

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CEREBRAL ANEURYSMS

Cerebral aneurysms are pathologic cerebrovascular system focal dilatations prone to rupture. The exact pathophysiology of their development, is still controversial [1-3]. Unlike the extracranial blood vessels, the brain ones have less elasticity in the tunica media and adventitia, they have less muscle in the media, the adventitia is thinner and the internal elastic lamina is much more prominent [1-3]. Moreover, we have to consider that large cerebral blood vessels lie within the subarachnoid space, where there is a minimal supporting connective tissue. The characteristics over-listed may predispose to the development of aneurysms. Aneurysms tend to grow in areas where there is a curve in the parent artery, in the angle between the aneurysm itself and the branching artery (Fig. 1) [3, 4].

![Diagram of an aneurysm](image)

**Figure 1:** Saccular intracerebral aneurysm.

Most of aneurysms lie over or near the circle of Willis. More than 90% of them, can be found in one of this following sites [1-3]:

a) internal carotid artery at the level of the posterior communicating artery;
b) junction of the anterior cerebral and anterior communicating arteries;
c) proximal bifurcation of the middle cerebral artery;
d) junction of the posterior cerebral and basilar arteries;

e) bifurcation of the carotid artery into anterior cerebral and middle cerebral arteries.

Other aneurysm sites on the carotid artery are over the ophthalmic, superior hypophyseal, and anterior choroidal arteries. There are other sites on the vertebral and basilar arteries, including those over the anteroinferior cerebellar, posteroinferior cerebellar, and superior cerebellar arteries and basilar and vertebral arteries junction [4].

Saccular, berry, or congenital aneurysms constitute 90% of all cerebral aneurysms and are located in the major branch points of large arteries [3]. Dolichoectatic, fusiform, or arteriosclerotic aneurysms are elongated outpouchings of proximal arteries that account for 7% of all cerebral aneurysms [3]. Infectious or mycotic aneurysms lie peripherally and comprise 0.5% of all cerebral aneurysms [3]. Other peripheral lesions include neoplastic aneurysms, rare sequelae of embolized tumor fragments, and traumatic aneurysms [3]. Traumatic injury also may result in dissecting aneurysms in proximal vessels [3].

If incidence is difficult to evaluate, we know that autopsy prevalence of aneurysms is about 2% [1-5]. The annual incidence of aneurismal subarachnoid haemorrhage (SAH) is about 6-8/100,000, with peak age between 55-60 years, and about 20% of cases occur between ages 15-45 years old [1-5]. SAH may be accompanied by intracerebral hemorrhage (20-40%), intraventricular haemorrhage (13-28%) and subdural blood (2-5%). About 50% of patients with aneurysms have warning symptoms, usually 6-20 days before SAH [5], with lateralized headache in 30% of cases, most in the side of the aneurysm. Soft evidence suggests that rupture incidence is higher in spring and autumn. Risks factors for SAH are hypertension, oral contraceptives, smoking, excessive alcohol, pregnancy [3]. In the Table 1 is reported the risk of rupture over 5 years according to International Study of Unruptured Intracranial Aneurysms [6].

The optimal treatment of aneurysm depends on several factors, such as aneurysm anatomy, surgeon ability, and patient general condition [1-5]. When treatment is
indicated, surgical clipping is considered the “gold standard”. Surgery target is to place a clip across the neck of the aneurysm to exclude it from the circulation without occluding normal vessels. When aneurysm cannot be clipped because of the nature of the aneurysm, or patient poor medical condition, other options may be considered. Sometimes (e.g., fusiform basilar trunk aneurysms, aneurysms with significant branches arise from the dome, or part the neck within the cavernous sinus) it is required aneurysm wrapping or coating [1-6].

Other alternative treatments to clipping can be [1-6]:

a) Trapping: distal and proximal occlusion by clip or ligation, by balloon, or some combination. A bypass (e.g., EC-IC bypass) may associated to avoid ischemia.

b) Hunterian ligation: proximal ligation.

c) Endovascular treatment, with: Guglielmi coils, balloon embolization, stent positioning, flow diverter.

There are no randomized studies dealing with natural history vs. treatment options [7], and most data come from personal experiences or retrospective facts.

In the last 20 years, there have been advances in techniques and instrumentation for intracranial aneurysm exposure and obliteration. However, it seems that 32% of the patients, who underwent surgery, suffer a fatal outcome or some form of sequelae [6, 7]. Cerebral blood flow alterations (CBF) occur in subarachnoid haemorrhage [6, 7]. In 1977, Nilsson measured CBF in 207 patients with ruptured intracranial aneurysms by an intravenous isotope method [8]. He found a strong correlation between neurological deficits and the level of isotope counts and transit times of the intravenously injected radionuclides [8]. Primary brain damage due to subarachnoid haemorrhage (SAH) and to vasospasm are the major cause of mortality and morbidity; but surgery-related complications constitute 14% of the morbidity [6, 8].

Indeed, the surgical therapy of cerebral aneurysms carries several risks related to manipulation, accidental or intentional blood vessels clipping, or bleeding due to
premature aneurysm rupture, suggesting room for improvement in surgical procedures.

Today, intraoperative electrophysiological monitoring with somatosensory and motor evoked potential (SSEP and MEP) recording, and electroencephalographic (EEG) monitoring, are frequently used in aneurysm surgery, and they are the standard techniques used for assessing the level of cerebroprotective anaesthesia and monitoring ischemia during surgical manoeuvres.

Table 1: Rupture risk over 5 years (%), International study of unruptured intracranial aneurysms [6]

<table>
<thead>
<tr>
<th>Type of Aneurysm</th>
<th>&lt; 7 mm and No Prior SAH</th>
<th>&lt; 7 mm and Prior SAH</th>
<th>7 – 12 mm</th>
<th>13 – 24 mm</th>
<th>&gt; 24 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid cavernous</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.0</td>
<td>6.4</td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>0</td>
<td>1.5</td>
<td>2.6</td>
<td>14.5</td>
<td>40.0</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>2.5</td>
<td>3.4</td>
<td>14.5</td>
<td>18.4</td>
<td>50.0</td>
</tr>
</tbody>
</table>

CEREBRAL PROTECTION DURING SURGERY

“Neuroprotection” means treatments used to protect neural tissue from cellular events induced by oxygen deprivation or glucose, or both of them, to the brain [9, 10].

Neurons are particularly susceptible to ischaemic injury because they have a higher demand for energy and limited energy stores [9, 10]. The oxygen deficiency precludes aerobic glycolysis and oxidative phosphorylation. ATP declines, cell homeostasis is deranged, and cell death occurs within minutes [10]. All these events are the so-called cerebral infarction [3]. Surrounding this central core is the penumbra, where collateral flow quickly establishes a marginal reperfusion. Cells in the penumbra may remain viable for hours [3]. Over time, infarct grows in size because perifocal tissues are taken in the infarction process [3]. It means that infarction operates within a certain time, so it’s possible to save perifocal tissues by reperfusion or by use of pharmacological agents that support cells at risk over a critical period [10].

Important strategies in neuroprotection include maintenance of normoxia & adequate cerebral perfusion pressure, maintenance of mild hypothermia, timely
surgical intervention and other methods (such as mannitol) to reduce increasing intracranial pressure (ICP), and several methods of pharmacological neuroprotection [3, 10].

In the anesthesiological management it’s important that blood pressure and volume should be kept normal or high [11-14] because vasospasm, which is the main cause of death and disability in patients surviving the initial hemorrhage, may be prevented by hypertensive and hypervolemic therapy [15-17]. A strong hypocapnia should be avoided to prevent cerebral vasoconstriction in areas at risk of vasospasm [16, 18].

The central nervous system ischemic tolerance may be enhanced by [3]:

1. *Drugs that mitigate the toxic effects of ischemia* without reducing cerebral metabolic rate of oxygen consumption (CMRO$_2$), such as: calcium channel blockers (nimodipine, nicardipine, flunarizine), free radical scavengers (superoxide dismutase, dymethylthiourea, lazaroids, barbiturates, vitamin C) and mannitol [3]. Although mannitol is not a cerebral protectant *per se* it has some potentially beneficial effects, such as osmotic diuresis, increased blood viscosity and free radical scavenging [19], reducing tissue damage caused by superoxide radicals [10].

2. *CMRO$_2$ reduction* by reducing the electrical activity of neurons [3]. With EEG monitoring anaesthetic agents (*e.g.*, barbitures, etomidate, propofol) may be titrated to the point of *burst suppression*.

3. Neurons maintenance energy reduction by mild *hypothermia* (warming/cooling blanket) [3].

Other cerebral protection techniques used in aneurysm surgery may be [3]:

1. *Systemic hypotension* [3]. Some surgical teams use it during the surgical dissection of the perforating arteries and in aneurysm manipulation for clip application [3]. Disadvantage of this method is that systemic hypotension may be harmful for possible dangers to
other organs and brain; so, this technique is not used by many surgical equips [3].

2. *Focal hypotension*, using temporary aneurysm clips (designed with low closing force to avoid intima injury) [3]. Temporary arterial occlusion allows to reduce intra-aneurysmal pressure, making easy the aneurysm dissection, and limiting cerebral ischemia to the territory of the parent artery [20]. It is useful in complex aneurysmatic lesions. However we think temporary occlusion should not be used, except when unavoidable, because of the possibility of causing ischemic brain damage. In fact it is good that temporary occlusion is associated to methods of cerebral protection against ischaemia. It may be combined with *systemic hypertension* to increase collateral flow [3].

3. *Circulatory arrest* [3]. Some teams use circulatory arrest in extreme situations, in patients with large, giant or complex aneurysms containing significant atherosclerosis and/or thrombosis that inhibits clip closure and a dome that is adherent to vital neural structures [3]. In this instance, adenosine is usually used.

Adenosine has a negative cardiac dromotropic and chronotropic effect; it typically takes effect within a minute after its administration. Heart rate gradually slows for about 20 to 30 seconds before asystole is reached for a mean time of 15 seconds, after which the heart rate begins to increase until a return to baseline in about 20 to 30 seconds.

**BRAIN PROTECTION: A MAJOR GOAL OF TREATMENT**

There are many surgical situations in which brain protection is considered a major goal of treatment.

In *carotid surgery*, many surgeons and anaesthesiologists, consider important the use of brain protection [10]. In the carotid endarterectomy cerebral ischaemia may be mainly associated to the formation and migration of emboli from the plaque, and to the decreased brain perfusion during clamping [10].
In cardiopulmonary bypass (CPB) two-thirds of patients present heavy neurologic deficit related to ischaemic insults due to microgaseous or thrombotic emboli [10, 21].

Another procedure in which cerebral protection is essential, is that of deep hypothermic circulatory arrest (DHCA) [10]. DHCA is used to help surgery in complex congenital cardiac malformations, aortic arch repair and giant intracerebral aneurysms of the posterior circulation [10, 22]. However the time available is very limited before a cerebral ischemic event arises [22]. The safe period for DHCA is generally considered to be 60 minutes or less [10]. Svensson et al. reported that a cerebral ischaemic time exceeding 45 minutes is associated with a high risk of stroke [10, 23].

Another situation in which the cerebral protection becomes crucial is the cerebral aneurysm surgery [10]. In this operation, feeder vessel temporary clamping may become useful to reduce intra-aneurysmatic pressure, to help in aneurysm dissection, to control bleeding or to help the proper placement of the final clip. However, this practice is complicated by certain risks, as the injury to the vascular endothelium and the ischemic damage to the brain in the area supplied by the artery that is interrupted [10].

Barbiturates have been widely studied and histological evidence of their brain-protection capabilities has been documented [24-27]. However, the myocardial suppression and the peripheral vasodilatation due to barbiturates, which may produce hypotension and compromise cerebral perfusion pressure (CPP), lead the research to other agents with similar capability protection and fewer side-effects [10, 24-27].

Lavine et al., in their series, used propofol and etomidate with reductions of cerebral metabolic rate of oxygen and the production of a burst-suppression pattern on EEG monitoring [29]. The authors noted that although these anesthetics have serious side-effects, they seem to have less effect on blood pressure than high-dose barbiturates [29].

Several experiences are reported in literature with different drug association for enhancing neuroprotection. For example in temporary focal occlusion during clip
ligation, Samson et al. used etomidate [28], Charbel et al. used an anaesthetic protocol of mannitol and pentobarbital bolus [30], and Ogylvy used a protocol of hypothermia, induced hypertension, and intravenous mannitol [31].

**USEFUL DRUGS IN ANEURYSM SURGERY**

**Papaverine**

Papaverine is particularly known as a smooth muscle relaxant and vasodilator. Indeed, it is an opium alkaloid antispasmodic drug, used as a nonspecific vasodilator of smooth muscles of the arterioles and capillaries [32].

Papaverine hydrochloride is a white, crystalline powder, odourless, with a slit bitter taste and it is soluble in water. Chemically, it is a isoquinoline, 1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxy-hydrochloride. Its classic structural formula is given below (Fig. 2).

![Papaverine structural formula](image)

**Figure 2:** Papaverine, structural formula ($C_{20}H_{21}NO_4$). Its IUPAC (International Union of Pure and Applied Chemistry) name is 1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxy-isoquinoline.

**Papaverine Drug Composition and Form**

Solution for injection. One ampoule of 1ml (2%) contains 20 mg of papaverine hydrochloride (20 mg/ml).

**Papaverine Medical Applications**

Papaverine is used as a muscular relaxant in acute peripheral arterial spasms: acute renal, biliary, and gastrointestinal colic. The drug is suitable as a cerebral
and coronary vasodilator in subarachnoid haemorrhage (combined with balloon angioplasty) [33] and coronary artery bypass surgery [34]. Papaverine may also topically applied to counter the mechanical vasospasm, resulting from vessel manipulation in operative procedures.

It may be also used in erectile dysfunctions, as a monotherapy or in association with α-adrenergic blockers, including phentolamine [33, 34].

Moreover, papaverine is commonly used in blood vessels cryopreservation with the other glycosaminoglycans and protein suspensions [35, 36]. Its use is also being investigated as a topical growth factor in tissue expansion with some success [37, 38]. It is used as an off label prophylaxis of migraine headaches too [37, 39].

**Mechanism of Papaverine Action**

Papaverine is a nonspecific phosphodiesterase inhibitor that increases cAMP and cGMP levels [32]. It may also alter mitochondrial respiration.

It has also been demonstrated that papaverine seems to be a selective phosphodiesterase inhibitor for the PDE10A, which is almost exclusively expressed in the striatum [40]. Subsequent increase in cAMP and cGMP after PDE10A inhibition seems to be "a novel therapeutic avenue in the discovery of antipsychotics" [40].

**Barbiturates**

Barbiturates are barbituric acid derivatives (malonyl urea), which is formed from malonic acid and ureabarburate. These drugs act as central nervous system depressants, especially in some brain portions, though they reduce the functioning of all body’s tissues [3].

**Barbiturates Medical Applications**

Barbiturates act depressing the central nervous system, so they may produce many effects, from mild sedation to total anesthesia. Most of them have a sedative effect in small doses and a hypnotic effect in larger ones. Barbiturates have anticonvulsants and analgesic effects too [3, 10, 41].
Nevertheless, barbiturates may be classified for their duration of action. Effects of long-acting barbiturates (e.g., barbital and phenobarbital) may last for as long as 24 hours; these drugs are used with other drugs as anticonvulsants [42]. Barbiturates of intermediate duration of action (amobarbital and butobarbital sodium) act for 6 to 12 hours and they are used in insomnia treatment [42]. Short-acting barbiturates (pentobarbital and secobarbital) are used to overcome trouble sleeping [42]. Ultrashort-acting barbiturates (thiopental sodium and thiamylal) are used intravenously and they are useful as induction agents, as supplemental drugs only during short periods when surgery requires increased depth of anaesthesia, or as maintenance hypnotics for short surgical procedures [42]. Barbiturates have largely been replaced as sedatives by benzodiazepines and other minor tranquilizers.

**Barbiturates and Anesthesia**

Barbiturates can reduce the CMRO\textsuperscript{2} and they can act like free radical scavengers [3, 10]. They produce dose-dependent EEG suppression which can be taken to isoelectric [3].

Moreover myocardial suppression and peripheral vasodilatation caused by barbiturates may produce hypotension and compromise cerebral perfusion pressure (CPP) above all in hypovolemic patients [3].

**Barbiturates Action**

Barbiturates, as well as the benzodiazepines, the zolpidem, and many other drugs bind to molecular components of the GABA\textsubscript{A} receptor present in neuronal membranes in the central nervous system [41-43]. This receptor, which acts as a chloride ion channel, is activated by the inhibitory neurotransmitter GABA [41-43]. The GABA\textsubscript{A} receptor has a pentameric structure (Fig. 3) assembled from five subunits (each with four transmembrane-spanning domains) selected from multiple polypeptide classes (\(\alpha, \beta, \gamma, \delta, \epsilon, \zeta, \eta, \text{etc.}\)). Different subunits of several of these classes have been characterized, for example six different \(\alpha\), four \(\beta\), and three \(\gamma\) [41-43]. A major isoform of the GABA\textsubscript{A} receptor found in many brain regions is two \(\alpha 1\) and two \(\beta 2\) subunits and one \(\gamma 2\) subunit [41-43]. Barbiturates interact with GABA\textsubscript{A} receptor isoforms that contain \(\alpha 1\) subunits (BZ1 subtype).
and they potentiate the effect of GABA at this receptor [41-43]. Barbiturates produce their pharmacological effects by increasing duration of chloride ion channel opening at the GABA<sub>A</sub> receptor and this increases the efficacy of GABA [41-43]. Barbiturates toxicity increase is due to the direct chloride ion channel gating or opening [41, 42]. Moreover, in addition to this GABA-ergic effect, barbiturates stop the AMP<sub>A</sub> receptor, a glutamate receptor subtype. CNS-depressant effects can be explained by the fact that barbiturates potentiate inhibitory GABA<sub>A</sub> receptors and inhibit excitatory AMP<sub>A</sub> receptors. At higher concentration, they inhibit the Ca<sup>2+</sup>-dependent release of neurotransmitters [43].

Further, barbiturates are non-selective compounds that bind to a superfamily of ligand-gated ion channels, of which the GABA<sub>A</sub> receptor channel is only one of several representatives [41-43]. This superfamily of ion channels includes the neuronal nACHR channel, the 5HT3R channel, the GlyR channel and others [41-43].

![Barbituric acid, structural formula](Image)

**Figure 3:** Barbituric acid, structural formula (C<sub>4</sub>H<sub>8</sub>N<sub>2</sub>O<sub>3</sub>). Its IUPAC name is 1,3-diazinane-2,4,6-trione.

**Barbiturates Adverse Reactions**

Barbiturates prolonged use —especially secobarbital and pentobarbital—may cause development of a tolerance to them and an increase of the dose needed to maintain symptomatic improvement or to promote sleep [41-43]. An overdose of barbiturates can result in coma and even death due to severe depression of the central nervous and respiratory systems [41-43].

Alcohol greatly intensifies the depressant effect of barbiturates, and in the 1950s and ’60s, barbiturates taken with alcohol became a common agent in suicide cases [41-43].
Barbiturates and Intraoperative Electrophysiological Monitoring

Thiopental use causes transient decreases in amplitude and increases in latency in cortical response after induction. Studies made with another barbiturate, phenobarbital, demonstrate that SSEP is unaffected at doses that produce coma [44], and changes are not seen until doses are sufficient to produce cardiovascular collapse [45]. Barbiturates are not used in MEP recording because the compound muscle action potential (CMAP) responses are unusually sensitive to barbiturates [46]. Furthermore, effects appear to be quite prolonged. In Sloan and Heyer study, induction bolus eliminated the CMAP from the MEP for a period of 45 to 60 minutes [46].

Etomidate

Etomidate is a short anaesthetic intravenous acting agent discovered at Janssen Pharmaceutica in 1964; it was introduced as an intravenous agent in 1972 in Europe and in 1983 in United States [47].

Etomidate Medical Applications

Etomidate can be used in anesthesia induction in patients with limited cardiovascular reserve, because it causes minimal cardiovascular and respiratory depression than other intravenous agents [50]. It is also indicated to supplement low-potency anesthetics, such as nitrous oxide and oxygen.

Because of it seems that etomidate may inhibit excitatory neurotransmitters release and may reduce CBF and ICP acting as cerebrovasoconstrictor, some neuro-anesthetists use etomidate for cerebral protection in aneurysm surgery [3, 10]. Disadvantages: it may be epileptogenic and may cause adrenocortical suppression (hypoadrenalism) [3].

Etomidate Chemistry

Etomidate is a carboxylated imidazole (ethyl ester of 1-(α-methylbenzyl) imidazole-5-carboxylic acid), whose classic structural formula is given below (Fig. 4).

The formula by which the etomidate is presented is a clear colourless solution for injection containing 2 mg/ml of etomidate in an aqueous solution of 35%
propylene glycol. However a lipid emulsion preparation has also been introduced. Etomidate is presented as a racemic mixture, but only the D-isomer has pharmacological activity.

Figure 4: Etomidate, structural formula \( \text{C}_{14}\text{H}_{16}\text{N}_{2}\text{O}_{2} \). Its IUPAC name is ethyl 3-[(1R)-1-phenylethyl]imidazole-4-carboxylate.

**Etomidate Action**

Etomidate is a modulator at GABA\(_A\) receptors [48] containing \( \beta 3 \) subunits [49]; it appears to have GABA–like effects. Unlike barbiturates, etomidate reduces subcortical inhibition at the onset of hypnosis while inducing neocortical sleep. It seems that etomidate acts in the depression of the activity and reactivity of the brainstem reticular formation.

**Etomidate Pharmacokinetic**

Etomidate produces a quick loss of consciousness, with minimal hypotension and unchanged heart rate [50]. Etomidate distribution is rapid, with a biphasic plasma concentration curve showing distribution half-lives of 3 and 29 minutes [50]. It seems that the short duration of its anesthetic effects is due to the drug redistribution from brain to highly perfused tissues [50]. Etomidate is extensively metabolized in the liver and plasma to inactive metabolites with only 2% of the drug excreted unchanged in the urine [50].

**Etomidate Side Effects**

Etomidate causes pain on injection and may produce muscle movements during its use as an induction anesthetic. It may also cause a postoperative nausea and vomiting. In addition, etomidate can suppress corticosteroid synthesis in the
adrenal cortex by reversibly inhibiting 11-beta-hydroxylase, an enzyme important in adrenal steroid production; it leads to primary adrenal suppression [51]. Because of etomidate-induced adrenal suppression, etomidate use for patients with sepsis is controversial [52-54]. Etomidate prolonged infusion in critically ill patients, may result in hypotension, electrolyte imbalance, and oliguria due to its adrenal suppressive effects. In addition, concurrent use of etomidate with opioids and/or benzodiazepines, is hypothesized to exacerbate etomidate related adrenal insufficiency [55, 56].

Etomidate consistently increases somatosensory evoked potentials amplitude (in contrast to most anaesthetic agents).

**Etomidate and Intraoperative Electrophysiological Monitoring**

Etomidate increases cortical SSEP components amplitude after injection without changes in subcortical and peripheral sensory responses [45]. Studies with MEPs have suggested that etomidate is an excellent agent in CMAP responses induction and monitoring [46]. Etomidate had the least degree of amplitude depression after induction doses or continual intravenous infusion. Thus, etomidate has been used for induction of anesthesia and as a component of TIVA, combined with opioids [46].

**PROPOFOL**

Propofol (2,6-diisopropylphenol) is a popular intravenous anesthetic. It is a short-acting sedative hypnotic. It has the property to reduce the cerebral metabolism, CBF and ICP [3].

**Propofol Medical Applications**

It is intravenously administered. It is used in general anesthesia induction and maintenance, procedural sedation (e.g., during endoscopic procedures), and sedation in mechanically ventilated adults.

Propofol is not considered as an analgesic; therefore opioids, such as fentanyl, may be combined with propofol to alleviate pain [57]. Postoperative nausea and vomiting are rare, because propofol has antiemetic actions [50].
It has some brain-protective properties in experimental incomplete ischemia [58], it allows a more rapid and “clear” recovery when compared with thiopental and isoflurane [59], and it has no adverse effect on adrenocortical function [60].

Its properties are responsible in propofol extensive use and some teams, including ours, prefer to use propofol in aneurysm surgery in anesthesia induction and maintenance and burst suppression. EEG research upon those undergoing general anesthesia with propofol finds that it causes a prominent reduction in brain's information integration capacity at gamma wave band frequencies [61].

**Propofol Chemistry**

Propofol was first marketed by Imperial Chemical Industries (now Astra-Zenica) in 1977 as a drug called Cremophor EL. Because of many anaphylactic reactions with Cremophor, the drug was pulled from the market. Shortly, after the emulsified formulation was re-marketed by ICI (1986) under the brand name Diprivan (abbreviated version of diisopropyl intravenous anesthetic). The currently available preparation is 1% propofol, 10% soybean oil, and 1.2% purified egg phospholipid (emulsifier), with 2.25% of glycerol as a tonicity-adjusting agent, and sodium hydroxide to adjust the pH [43, 50]. Due to the high volume of oil (10%) and water (89%), the oil’s total emulsion in the solution causes a look like milk liquid.

Diprivan contains ethylenediaminetetraacetic acid, shorted as EDTA, whose classic structural formula is given below (Fig. 5). EDTA is a polyamino carboxylic acid family member of ligands; it usually binds to a metal cation through its two amines and four carboxylates. EDTA is known to be a powerful chelating agent, that also acts alone and synergistically with some other antimicrobial agents. Newer generic formulations of propofol contain sodium metabisulfite or benzyl alcohol as antimicrobial agents.

A water-soluble prodrug form, fospropofol, has recently been introduced. Fospropofol is rapidly broken down by the enzyme alkaline phosphatase to form propofol. This new formulation may not produce the pain at the injection site.
Figure 5: Propofol, structural formula (\([(\text{CH}_3)_2\text{CH}]_2\text{C}_6\text{H}_5\text{OH}\)). Its IUPAC name is 2,6-disopropylphenol.

Propofol Action

Propofol action involves an inhibitory positive modulation of the function of the neurotransmitter g-aminobutyric acid (GABA) through GABA\(_A\) receptors. Recently, propofol action has been associated [62-64] both to the potentiation of GABA\(_A\) receptor activity, so to the slowdown the channel-closing time, [65-67] and also as a sodium channel block [68, 69].

Propofol Pharmacokinetic

After intravenous administration of propofol, the distribution half-life is 2–8 minutes; the elimination half-life is approximately 30–60 minutes [43, 50]. The drug is rapidly metabolized in the liver (ten times faster than thiopental) and excreted in the urine as glucuronide and sulfate conjugates [43, 50]. Less than 1% of the drug is excreted unchanged [43, 50]. Total body clearance of the anesthetic is greater than hepatic blood flow, suggesting an extrahepatic site of elimination as well. This property is useful in patients with impaired ability to metabolize other sedative-anesthetic drugs.

Its characteristics of rapid onset and recovery along with its amnestic effects [71] have led to its widespread use for sedation and anesthesia.

Propofol Side Effects

Propofol effects on respiration are similar to those of thiopental at usual anesthetic doses [50]. However, propofol causes a significant reduction in systemic blood pressure during anesthesia induction, first through decreased peripheral resistance [50]. In addition, propofol has greater negative inotropic effects over the heart than etomidate and thiopental. However, although propofol decreases systemic vascular resistance, reflex tachycardia is not observed [42]. Heart rate stability produced by propofol relative to other agents is likely the result of either resetting
or inhibiting the baroreflex, thus reducing the tachycardic response to hypotension [42].

Apnea and pain at the site of injection are adverse effects of bolus administration. Muscle movements, hypotonus, and (rarely) tremors have also been reported following its use [50].

**Propofol and Intraoperative Electrophysiological Monitoring**

Propofol-induced unconsciousness in humans is associated with thalamic inhibition activity evoked by somatosensory stimuli [72, 73]. Thalamus is central in sensory information processing and transfer that last reaches the cortex, with the exception of olfaction, whose signals pass to the cortex without thalamic relay [72, 73].

*In vivo* extracellular studies have showed that propofol suppresses field potentials in rat thalamus and cortex, with more prominent effects in the cortex [74]. However, cortical suppression may reflect anesthetic actions on projection neurons located in other positions, especially in the thalamus [75, 76].

Thalamus studies, in which has been made use of a wide variety of techniques (including electrophysiology, gene knockout, immunohistochemistry, immunoprecipitation, and ligand binding), it has been suggested that ventro-basal (VB) neurons primarily express synaptic $\alpha_1\beta_2\gamma_2$ and $\alpha_4\beta_2\gamma_2$ and extrasynaptic $\alpha_4\beta_2\delta$ GABAA receptors while reticular thalamic nucleus (RTN) neurons are likely preferentially express synaptic $\alpha_3\beta_3\gamma_2$ GABAA receptors, with denser GABA receptor expression in VB than in RTN [40-58]. These data support the hypothesis that thalamus represents a propofol important anatomic target. Shui-Wang Ying and Peter A Goldstein, demonstrated that, switching thalamic somatosensory inhibition relay neurons by propofol at clinically relevant concentrations is primarily mediated through the potentiation of the GABAA receptor chloride channel-mediated conductance, and such inhibition may contribute to the impaired thalamic responses to sensory stimuli seen during propofol-induced anesthesia [77].

In studies with MEPs, authors noted a depressant effect on response amplitude, consistent with a cortical effect [78, 79]. Although propofol does not appear to
enhance cortical responses, its rapid metabolism allows rapid adjustment of the depth of anesthesia and effects on evoked responses. In TIVA, propofol infusions have been combined with opioids and have produced acceptable conditions in monitoring SSEPs and MEPs [80, 81]. It has become a widely used agent in TIVA because of its quickly exposure [46].

**SOMATOSENSORY AND MOTOR SYSTEMS ANATOMY AND PHYSIOLOGY**

**Somatosensory System Anatomy and Physiology**

Somatosensory system subserves the fifth sense “Das Gefühl”, which is made by five submodalities: mechanoreception, thermoreception, nociception, proprioception and visceroreception [82]. Somatosensory afferents are involved in many motor and autonomous reflex pathways and feedback loops with reflex centers in the spinal cord, brainstem and forebrain [82].

Two sensory systems, the dorsal column-lemniscal system and the spinothalamic one, make up somatosensory system [82]. Both systems use three neurons to convey sensory information from peripheral sensory receptors to conscious levels of cerebral cortex. Dorsal column–lemniscal system subserves mechanoreception (fine touch, vibration, pressure, two point discrimination) and proprioception (joint position, movement and force) [82]. Spinothalamic tract system subserves thermoreception, nociception and visceroreception [82].

In both systems, the first sensory neuron that innervates a sensory receptor has a cell body in the dorsal root ganglion, the trigeminal ganglion, the midbrain trigeminal nucleus and the vagal ganglion nodosum [82]. The first neuron synapses with a second neuron in the dorsal column nuclei (lemniscal system) or in the spinal cord dorsal horn (spinothalamic tract system) [82]. Axons of the second neuron crosses the midline [82]. The second neuron axon synapses on a third neuron that is in the ventroposterior nuclei of the thalamus [82, 83]. The axon of the third neuron projects to somatosensory cortex areas, which include primary and secondary somatosensory cortex, posterior parietal cortex, posterior and mid-insula and mid-cingulate cortex [82, 84]. Moreover, other pathways have been suggested to be involved in mediating somatosensory functions, such as the dorsal spino- cerebellar tract (lower limb
proprioception), postsynaptic dorsal column pathway (pelvic organ pain), and vagus
nerve (non-painful visceral percepts) [82, 83].

**Motor System Anatomy and Physiology**

Corticospinal tract conveys voluntary skilled movements. First motor cortex is
located in frontal lobe precentral gyrus and in the premotor area, which is located
previously to the primary motor cortex. Together, they give rise to about 60% of
the fibers. Primary and secondary somatosensory cortical areas are located in
parietal lobe and they give rise to about 40% of the corticospinal tract fibers [83].

In corticospinal tract, fibers leave cerebral cortex in internal capsule, which carries
axons in and out from the cortex [83]. Corticospinal fibers, then, come down through
brain stem length, in midbrain ventral portion, pons and medulla [83].

In lower medulla, 80 to 90% of the corticospinal fibers cross at the decussation of
the pyramids and continue in the contralateral spinal cord as the lateral
corticospinal tract [83]. Lateral corticospinal tract descends in the side part of
spinal cord white matter. As it comes down, axons leave the tract and enter the
ventral horn gray matter to synapse on lower motoneurons [83].

**Brain Electrical Activity**

Electroencephalograph may record spontaneous electrical activity generated in the
cerebral cortex. This activity reflects the electrical currents that flows in the brain
extracellular spaces, and these reflect the effects of innumerable excitatory and
inhibitory synaptic potentials upon cortical neurons [85]. Cortical neuron activity is
influenced and synchronized by subcortical structures, particularly by thalamus and
high brainstem reticular formation [85]. Afferent impulses from these deep
structures are probably responsible of entraining cortical neurons to produce typical
rhythmic brain-wave patterns, such as alpha rhythm and sleep spindles [85].

**Monitoring Somatosensory Evoked Potentials**

Somatosensory evoked potentials (SSEPs) are used to evaluate both central and
peripheral nervous systems, confirming lesions in somatic sensory systems,
helping to localize them, and providing a prognostic guide [82]. Today, SSEPs are
not only used in clinical neurophysiology laboratories but other special clinical applications have been introduced, such as intraoperative monitoring and recordings in intensive care unit [82].

In operative room (OR), SSEPs may be used to prevent neurological impairment, by identifying them, to allow prompt correction; moreover intraoperative SSEPs may be helpful to follow-up induced physiological changes, and to locate the central sulcus [82, 86].

As a preventing instrument of neurological damage, SSEPs are sensitive to two important physiopathological events: mechanical stretching/damage and ischemia [82]. SSEPs often predict motor outcome because in most instances ischemia affects sensory and motor pathways simultaneously; medial lemniscus ischemia in thalamus or the thalamocortical projections rising through internal capsule posterior limb and corona radiata should cause SEP attenuation [87]. Meldrum and Brierly in 1967 were the first to suggest the use of SSEPs for ischemia research. In the last decade, the relationship between SEPs and cortical blood flow (CBF) has been investigated by Branston and Symon's group [88-90]. Most previous work, including theirs, suggests that the amplitude of cortical SSEP waves is closely associated with ischemia; latency changes are more variable [88-90].

Acute compression first causes a drop in conduction velocity, which may be followed by complete conduction block within some tens of minutes [82]. Beyond disappearance of upstream peaks, nervous disruption may cause the “killed-end effect”, that is the appearance of high-amplitude positivities immediately rostral to the lesion [82].

Several investigators have applied SSEPs as a method of monitoring the functional effects of decreased blood flow both in the clinical and experimental setting [91-93]. Indeed, SSEPs monitoring has been widely employed in intracranial vascular surgery [94-96], because they are easily recordable and do not require particular anesthesiological regimen adaptation [82]. It proved SSEPs are particularly useful and they influenced the surgery in complicated cases, such as giant aneurysms, permanent vessel occlusion, and temporary clipping [97].
SSEPs changes in a target cerebral artery area in unsafe conditions, like critical brain retraction, mechanical vasospasm, temporary occlusion, troubles in perforating vessels, and low aneurysms clipping, may help neurosurgeons to adapt surgical strategy and avoid ischaemic damage [20, 98, 99].

Several studies noted that SSEPs assessment in response to tibial nerve stimulation, may be a reliable index of ischemia occurring in anterior cerebral artery (ACA) territory; while median nerve SSEPs reflect cerebral blood flow (CBF) in the middle cerebral artery (MCA) territory and the a rapid disappearance of N<sub>20</sub> component is a danger signal [100].

On the other hand, literature reports a false negative rate up to 25% [100-102] about new postoperative motor deficit incidence in SSEP monitoring, suggesting that combined SSEP and MEP intraoperative monitoring is superior to SSEP monitoring alone in predicting ischaemic events caused by blood flow of some perforating arteries disturbance [99, 103-106].

**Tibial Recording and Median Nerve Somatosensory Evoked Potentials During Aneurysm Surgery**

In this section, we report our method of SSEP recording that we apply in operating room during aneurysm surgery, according to many authors in the current literature [107].

Neurophysiological recordings are usually continuously performed from the opening of the dura mater until its closure. All the data are collected by Epoch XP/Eclipse equipment (Axon Systems Inc. Hauppauge, NY, USA).

SSEPs are usually elicited by stimulation of right and left median nerve at the wrist and right and left posterior tibial nerve at the ankle using disposable subdermal twisted pair needle electrodes. Regular pulses are delivered adjusting intensity to a visible muscle twitch (range: 20-30 mA lasting 500 ms at the rate of 4/s). Evoked potentials are recorded through disposable screw needle electrodes placed on the scalp at C3’, C4’ and Cz and at the CVII vertebra with a reference electrode placed at Fpz. The ground electrode is placed above an arm. An analysis time of 100 ms is used for each SSEP to detect waves after N20-P25 complex, which are much more sensible to hemodynamic and anesthesiologic variations.
N20 latencies (median nerve) and P40 (posterior tibial nerve) and N20-P25 amplitude and P40-N50 are noted. A pathologic event standard, in the SSEP, is defined in three degrees: 1) intracortical middle latency components amplitude decrease and latency increase after N20-P25 complex (grade 1), 2) amplitude reduction below a threshold of 50% or the increase of latency by 10% of the N20-P25 complex (grade 2), 3) P25 disappearance in decreasing amplitude of N20 more than 70% and latency reduction more than 10% respect to baseline (grade 3). Changes in SSEPs are reliable if they are repeatable and sustained at least two consecutive acquisitions. In pathologic event of first-second degree, surgeon is warned and any changes in anesthesia or hemodynamic parameters are promptly adopted; in pathologic event of second-third degree, a removal prompt or clip readjustment is required to surgeon (Fig. 6).

![Figure 6 (A-C): Example of SSEP monitoring during surgery for AcoA cerebral aneurysm in our Institute. During the position of the definitive clip we noted grade 1 alteration of lower SSEPs mainly on right side (A), with recovery after systemic blood pressure was increased of 30% (B). Normal SSEPs at the end of the surgical maneuvers (C). “TIBS” stand for “tibial nerve stimulation” (measured at electrode contact hardware).](image-url)
Motor Evoked Potentials

In this years, MEP monitoring has gained a wider consensus as a supplementary technique to detect perforating vessel compromise, which may lead to motor impairment not reflected by SSEPs [87, 98, 104, 105, 108-110], especially in subcortical ischaemia, because of the lenticulostriate arteries and anterior choroidal artery [105, 109]. MEP changes reflect ischaemic events at the pyramidal tract, and detection of MEP changes and surgical manoeuvres adjustment prevent irreversible pyramidal tract damage [87]. Several investigators have analyzed the relationship between MEP changes and postoperative motor function [98, 104, 109-111]. Depending on the individual vascular supply and collateralization, MEP disappearance for more than 10 min is suggestive of a post-operative motor deficit [87, 109, 110].

Traditionally, it is known that anesthetics, in particular the halogenated inhalational agents, may oppose MEP recording. For this reason, neuroanaesthesiologists prefer a total intravenous anesthesia with propofol, and an opioid when performing MEPs [112].

Two main techniques are involved for MEP monitoring in aneurysm surgery: transcranial electrical stimulation (TES) and direct cortical stimulation (DCS).

TES allows an easy, fast and less invasive monitoring of the motor pathways, but it has two major disadvantages: muscles twitching interfering with crucial parts of the surgery, and the risk to by-pass the subcortical ischemia when an high/excessive stimulus intensity, is applied to recruit the subcortical structures [110].

DCS MEP monitoring was born to avoid these kind of disadvantages. Indeed, this technique involves a direct cortical stimulation through a subdural strip electrode [110, 113]. Then a focal muscle activation, less movement, and superficial stimulation for detecting cortical and subcortical ischaemia are produced avoiding false negatives [87]. Also DCS MEP monitoring has some risks. Problems of technique are: risk vein rupture bridging, with subdural bleeding, related to the subdural strip electrode positioning (horiuchi, sakuma, Suzuki, szelenyi 2005), risk to danger cortex, especially in case of subarachnoid hemorrhage where
parenchyma is edematous [98], risk to realize a “too focal” activation and difficulty to reach the leg area [105, 108-110].

In our operating room, together with EEG and SSEP monitoring, we have so far used TES MEP monitoring, although we are working for the DCS MEP application.

MEP Recording in Aneurysm Surgery

TES MEP Recording in Aneurysm Surgery

In this section is reported our method in MEP recording applied in operating room.

Short sections of multiple pulses are used following the segmental alpha motor neuron summation (train of five square wave stimulations, 500 ms lasting at the rate pulse/s of 250, ISI: 4 ms) through disposable screw needle electrodes placed on the scalp at C1-C2 (according the 10-20 International system), to obtain placement over the motor cortex.

Once optimal stimulus parameters are established, 8 consecutive baseline MEPs are recorded in stable conditions of neuromuscular blockade, general anesthesia and physiological parameters (blood pressure, body temperature). At least, 30 s are allowed to elapse between two successive traits. MEP recording were repeated during critical times (such as temporary clipping of an artery or repeated clip placement during complex aneurysm clipping). Changes in MEPs are compared to the most reliable response and with the baseline measurement. MEP amplitude is measured peak to peak between two largest peaks.

In our experience, we considered a significant change, a persistent and consistent decrease in amplitude or a total abolishment. Reproducible amplitude decreases of $>50\%$ and latency increases $>10\%$ are considered to be a significant deterioration. In line with Guo [87], we used a combination of threshold and amplitude as part of the alarm criteria consisting of either an increase in motor threshold of more than 20 mA and/or more than 50% amplitude decrease in the response.
DCS MEP Recording During Aneurysm Surgery

In DCS MEPs, a strip electrode is inserted into subdural space parallel to and over the precentral gyrus, with the laterally-located contacts over the arm and hand motor areas, and medially-located contacts over the leg motor area [87]. An electrode placed at Fpz act as a cathode [108-110]. The electrode with the lowest stimulation threshold, for a contralateral muscle response corresponding to the vascular territory of interest, is chosen for continuous MEP monitoring [87].

EEG

Multimodality neuromonitoring facilitate tailoring neuroprotection protocols to various clinical circumstances. So, it’s possible an application of a most appropriate means for correcting an imbalance; electroencephalography has been used to assess the brain electrical activity [10].

It is well known that a cerebral blood flow stop causes a interruption of neural activity, followed by cellular death within a few minutes [114]. Pathogenetic relevance of this event is related to the residual blood flow and to the duration of the ischemia, whose entity is not easily measurable in clinical practice [114]. Then, several studies have been performed in describing a correlation between EEG changes and cerebral blood flow (CBF) variation [114-118]. The relationship between CBF and changes in the EEG was studied in patients undergoing carotid endarterectomy, highlighting a link between changes in flow and changes in the EEG [114, 117]; flows of less than 17 ml/100 gm/min were invariably associated with marked changes in the EEG [117]. Results reported in literature indicate that computerized EEG monitoring in aneurysm surgery may have value in early detection of intraoperative cerebral ischemia. During this surgery, feeder vessel temporary clipping may become necessary to control bleeding or for proper placement of the final clip [10]. Obviously, this exposes to a high risk of accidental occlusion of the perforating arteries and/or undesirable and extremely dangerous flow decrease to the distal territories. The same risks of the perforating vessel occlusion exist during the simple dissection of the aneurysm and the final clipping. Therefore, a full and real time flow monitoring is to be considered mandatory in aneurysms surgery.
The direct cortical response (DCR) can be monitored on line second by second, and it can be measured from any site of cerebral cortex [119]. EEG recordings allow to identify abnormal cerebral blood flow changes by means of visual analysis or by a sophisticated and objective computerized examination of specific parameters. EEG spectral changes are mainly taken into account. Alpha band activity modifications plays an important role in the dynamics of ischemia [114]. Several investigators noted a decrease in relative alpha and beta band power associated with an increase in slower frequencies power [120, 121]. A decrease in long-term variability of the alpha power has been described in vascular spasms occurring in subarachnoid haemorrhages [122].

Furthermore, anaesthesia of a patient in acute phase, can be monitored with EEG since interburst interval or bursts per minute can be calculated.

**EEG and Burst Suppression**

The burst suppression (BS) pattern is a peculiar signal in the EEG. It is characterized by a periodic pattern of low voltage less than 10 $\mu$V and a relatively shorter pattern of higher amplitude complexes (Fig. 7).

![Figure 7: Example of 78% burst suppression.](image)

Doyle PW & Matta BF demonstrated that there is a greater reduction in cerebral blood flow with a completely isoelectric EEG than with 50% burst suppression [123]. They noted also that there is a significant decrease in middle cerebral artery flow velocity with increasing EEG, but jugular bulb venous saturations did not change consistently with the change in EEG activity, indicating intact flow-metabolism coupling [123]. They concluded that the degree of EEG suppression
had a significant effect on blood flow and, if suppression of metabolic activity has a part in cerebral protection, complete EEG silence may give more protection than 50% burst suppression [123].

**EEG Recording During Aneurysm Surgery**

In this section, we report our method EEG recording, applied in operating room in aneurysm surgery. EEG signals were recorded continuously using disposable screw needle electrodes placed on the scalp at Fp1-Fp2-(F3-F4)-C3-C4-P3-P4-(T3-T4)-O1-O2 according to the 10-20 International System. A 8 channels montage with Fpz as common reference was used. Proper arrangement was performed according to the needs of the craniotomy. Electrodes for EKG and from the skin of the face were placed to detect mechanical artifacts due to surgical maneuvers. Band pass was 1-40 Hz, sensitivity was 5-7uV/mm depending on the phases of monitoring, paper scroll was 15 mm/sec. Electrode impedance was maintained less than 5 Kohms. Furthermore, EEG was analyzed in frequency domain by means of non parametric methods based on Fast Fourier Transform (FFT) using a two second sample (epoch) of EEG with an averaging time of 20 s and updating rate of 25 s. 128 spectral points were calculated within a total frequency band from 0 to 32 Hz. The spectrum was then separated into frequency bands based upon definitions made in the bands area (Delta: 0.5-3.5, Theta: 3.5-7.5, Alpha: 7.5-13, Beta1: 13-21.5, Beta2: 21.5-32). System automatically calculated the following measures for each band: Absolute power of each frequency band. Relative power (percent in each frequency band relative to the total band), Root Mean Square (RMS) as the voltage of the EEG in each band, Peak frequency in Hz of the highest power bin in the band, Mean frequency as the frequency within each band that divides the absolute power such as 50% of the power is above and 50% below the mean frequency. For each EEG trace were also calculated: Burst Suppression Ratio (BSR) and Spectral Edge Frequency (SEF). BSR is tim percentage that EEG epoch is in suppressed phase of Bursts Suppression activity. Default total analysis time was 4s, the minimum suppression time (the time the EEG must be below the suppression threshod) was 240 ms, the suppression threshold (the voltage for determination of the suppressed EEG phase) was 5 microV. SEF for the total frequency band is that frequency below which the spectra contains a specified percentage of power defined by the SEF.
Our default value was 95%. Datas were collected and visualized as numeric values and also displayed in Compressed Spectral Array (CSA) mode. According to Blume, we defined two degrees of abnormalities provoked by ischemia due to clamping of cerebral arteries: 1) minor abnormalities (reduction of 8-15 Hz activity of more than 50 % and increase of delta activity superior to 1Hz), 2) major abnormalities (disappearence of alfa-beta activity with increase of delta activity inferior to 1Hz. We also considered amplitude and asimmetry suppression between the two emispheres [124].

Anesthetic Recommendations for Intraoperative Monitoring of Evoked Potentials (EPs) During Aneurysm Surgery and our Practice

The impact of anesthetic agents on neurophysiologic monitoring increases with the number of synapses in the pathway monitored, because anesthetic agents produce effects altering neuronal excitability through changes in synaptic function or axonal conduction [46, 125-127]. Therefore, visual evoked potentials are very sensitive to interference by anesthetics, whereas brainstem auditory evoked potentials are essentially unaffected by anesthetics. Somatosensory evoked potentials (SSEPs) are intermediate in sensitivity, and transcranially evoked motor evoked potentials (MEPs) are particularly challenging because of marked interference by anesthetic agents.

Some clinical studies [128-130] proved that inhaled anesthetics decrease amplitude of EP cortical components to a greater extent than predominantly narcotic-based general anesthesia [131]. Moreover, they have limitations to increase EP latency and slow down EEG. However, if inhanltoin anesthetic agents must be used, you should to avoid the use of halothane, isoflurane and Ethrane® [3], because effects mentioned above, are particularly evident. It should also be avoided benzodiazepines, and, during MEP monitoring, muscle relaxants agents [3].

At our institution for patients requiring intraoperative monitoring of EPs in aneurysm surgery, general anesthesia is induced with propofol (1%) and remifentanil (50µg/mL) using the Target Controlled Infusion (TCI) (BASE PRIMERA™, Fresenius, France).
General anesthesia was induced with propofol (1%) and remifentanil (50 µg/mL) using the Target Controlled Infusion (TCI) (BASE PRIMERA™, Fresenius, France). During the entire surgical procedure, basing on EEG, the effect-site propofol concentration (2 to 3.5µg ml⁻¹) (Schnider model) [132, 133] and remifentanil concentration (5 to 9µg ml⁻¹) (Minto model) [134] were maintained constant. Cisatracurium (0.1mg/Kg) was administrated only to facilitate endotracheal intubation. Patients were ventilated in volume control mode, with a mixture of 50% of O₂ and air, to ensure a systemic arterial oxygen partial pressure (PaO₂) of >100 mmHg and a systemic arterial CO₂ partial pressure (PaCO₂) of 35-40 mmHg. Moreover a warming/cooling blanket was used to maintain body temperature at 35-36°C.

Patients were placed supine with head and trunk elevated to facilitate venous outflow; therefore only SAH cases was administered mannitol 10% (0.25-0.5 g/Kg).

During the preparation of the approach and the microsurgical dissection, all patients were maintained hemodynamically stable, with MAP values of 50-60 mmHg in normotensive patients and values of 70-80 mmHg in hypertensive ones.

Any temporary occlusion of a cerebral artery required neuroprotective measures depending on the duration of occlusion. When the expected duration was less than 1 to 2 minutes, there was no need for interventions, but if the duration was likely to be longer, following interventions were performed:

1. A value of inspired [O₂] of 100%
2. Induced hypertension of about 20% above the basal MAP values through endovenous boluses of phenylephrine (25 to 100µg) or continuous infusion of noradrenaline. In case of SSEPs changes, the hypertension was induced of about 30% above the basal MAP values.
3. A value of burst suppression, on the EEG, of at least 80% through endovenous boluses (50-100mg) of propofol.

This same anesthesiologic management is achieved even in case of prophylactic use of temporary occlusion in aneurysmatic lesions.
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CONFLICT OF INTEREST

The author(s) confirm that this chapter content has no conflict of interest.

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