Gli stati della Coscienza e l'Anestesia

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MONITORING BRAIN FUNCTION DURING ANESTHESIA

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The operating room neurophysiology monitoring team should consist of:

- **Clinical neurophysiologist** (M.D., D.O. or Ph.D. qualified by training and experience, certified by an appropriate board such as the American Board of Clinical Neurophysiology)

- **Electroneurodiagnostic technologist** (qualified by training and experience)
The monitoring team should be under the supervision of clinical neurophysiologist, who has the overall responsibility for the conduct of the intraoperative monitoring procedure, including the interpretation of the intraoperative EEG.

The qualified clinical neurophysiologist should be available to offer interpretative advice, including during critical periods of monitoring (cross-clamping of great vessels, induction of progressive hypothermia, extracorporeal circulation).
Alterations in the EEG and the interpretation by the clinical neurophysiologist, are described to the surgeon.

Discussion between the surgeon and the neurophysiologic monitoring team usually should be conducted through the clinical neurophysiologist, and the surgeon should interpretate the EEG findings in clinical circumstances.

However, informations must be exchanged between various members of the operative team (nursing staff, anesthesiologist, surgeon, perfusion technician)
Intraoperative neurological monitoring Guidelines
ASE/SCA Guidelines for Performing a Comprehensive Intraoperative Multiplane Transesophageal Echocardiography Examination

Shanewise JS et al. 1999, 89:870

Savage RM

Authors: 90% Anesthesiologists
8% Cardiothoracic Surgeons
2% Cardiologists
• Demographic data
• Pathophysiology
• Pre-emptive strategies
• Neuromonitoring
Clinical neurologic deficits after CPB in adults have been reported to occur in 1% to 5% of patients. In contrast, the incidence of subclinical postoperative neurologic dysfunction in 50% to 70%
Classification

- **Type I**: - major focal neurological deficits
  - stupor
  - coma

- **Type II**: - deterioration in intellectual function
  - agitation
  - memory deficits, seizures, without evidence of focal injury

Eagle KA et al. ACC/AHA 2004 Guideline Update for CABG
Mortality

- 21% in patients with Type I neurological deficits
- 10% in patients with Type II neurological deficits

versus a mortality rate of 2% in patients with no adverse cerebral outcomes

Pathophysiology

• Hypoperfusion

• Micro- Macrovasculature embolization

• Systemic inflammatory response

Pathophysiological bases of CPB-derived brain damage

J. Murkin (London – Ontario) Intercept 2005
Pre-emptive strategies 1

• Selective use of preoperative carotid imaging and TEA
• Routine use of intraoperative TEE and EAE imaging
• Off Pump strategies
• Descending aortic cannulation with TEE guidance
• Femoral artery cannulation
• On cross-clamp proximal grafts anastomosis
• Descending thoracic aorta proximal anastomosis

Intraoperative pre-emptive strategies for limiting brain damage C. Schmitz (Bonn - Germany) Intercept 2005
Pre-emptive strategies 2

• High flow-high pressure CPB
• Coagulation and inflammatory response management during CPB
• pH management
• Temperature management
• Carbon dioxide instillation in chest cavity during open heart or Heart-Port procedures
• TEE guided deairing
• Ascending aortic device use (Embolex®)

Intraoperative pre-emptive strategies for limiting brain damage C. Schmitz (Bonn - Germany) Intercept 2005
Pre-emptive strategies 3

NEUROMONITORING

Monitoring brain function during CPB D. Colella
(Rome - Italy) Intercept 2005
The ideal neurophysiologic monitor should provide a noninvasive, continuous and objective method of rapidly assessing cerebral perfusion, oxygenation and activity.

The usefulness of neuromonitoring in preventing neurological complications relies on its ability to detect neurological disfunction at a reversible stage.

Deciding on the most appropriate choice of monitor or outcome measure has become a complex and often confusing process.
Jugular venous oximetry (S\textsubscript{jvO2})

There is a significant correlation between S\textsubscript{jvO2} and Xe\textsubscript{133} clearance

\[
\text{CMRO}_2 = \text{CBF} \times \text{a-jvDO}_2
\]

- **Normal oxygen extraction** of the brain is **30-40%**
- Normal range for **SjvO2 60-70%**
- Reduction in SjvO2 is a useful marker of inadequate CBF
- Arterio-jugular difference in oxygen content >9 ml/dl provides an useful marker of inadequate CBF

Sheinberg M et al. J Neurosurg 1992;76:212
Cruz J. Crit Care Med 1998;26:344
Indices of low cerebral blood flow

- SjvO2 <50%
- a-vDO2 >7.5 ml/dl
- Cerebral Extraction of oxygen >40%
<table>
<thead>
<tr>
<th><strong>Decrease in SjvO2</strong></th>
<th><strong>Increase in SjvO2</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Oxygen Delivery</td>
<td>↑ Oxygen Consumption</td>
</tr>
<tr>
<td>↑ ICP ↓ CPP</td>
<td>Increased metabolism</td>
</tr>
<tr>
<td>Excessive hypocapnia</td>
<td>Hypertermia</td>
</tr>
<tr>
<td>Vasospasm</td>
<td>Pain</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Light anaesthesia</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>Seizures</td>
</tr>
<tr>
<td>Cardio Resp. Insufficiency</td>
<td></td>
</tr>
<tr>
<td>Anaemia</td>
<td></td>
</tr>
<tr>
<td>Haemorrhage</td>
<td></td>
</tr>
<tr>
<td>Hb abnormalities</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td></td>
</tr>
<tr>
<td>↓ ICP ↑ CPP</td>
<td>Coma</td>
</tr>
<tr>
<td>Hypercapnia</td>
<td>Hypotermia</td>
</tr>
<tr>
<td>Drug vasodilation</td>
<td>Sedative drugs</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>Cerebral infarction</td>
</tr>
<tr>
<td>A-V malformation</td>
<td>Brain death</td>
</tr>
<tr>
<td>↑ PaO2</td>
<td></td>
</tr>
</tbody>
</table>
Long term neurologic and cognitive outcomes were not associated with intraoperative or postoperative SjvO2 desaturation

SjvO2 advantages

- Continuous, online monitor
- Allows calculation of a-vDO2
- Good correlation with cerebral dysfunction

SjvO2 limitations

- Invasive procedure
- Indicates global and not regional oxygenation
- Sampling can be contaminated
- The continuous fiberoptic catheters may give inaccurate readings (impacted against the vessel wall or thrombosys)
- Temperature influences the oxyhaemoglobin dissociation curve

NEAR-INFRARED SPECTROSCOPY (NIRS)

Monitoring of several markers of cerebral cortical oxygenation:

- HHb (deoxygenated Hb)
- O2Hb (oxygenated Hb)
- Cyt-Ox (redox status of the cytochrome c oxidase)
- TOI (tissue oxygenation index)
- THI (tissue haemoglobin index)
NIRS cerebral monitoring measures haemoglobin saturation of a small region of the cranial microvasculature

However the association between frontal cortex oxygen desaturation and neurocognitive decline has been independently confirmed

Yao FS et al. Anesthesiology 1999;91:A73
Monk TG et al. Anesthesiology 2000;93:A167
The majority of the contribution to the NIRS signal is likely to be from venous blood (as it contributes approximately 70% of the intracranial blood volume) 

Kirkpatrick PJ et al. J Neurosurg 1995;83:963

NIRS showed a higher specificity and sensitivity than jugular bulb oximetry in detecting cerebral desaturation

NIRS

• It is more reliable when monitoring trends rather than absolute values


• In contrast to EEG, which affected by anaesthetic agents, a decrease in rSO2 is caused by an imbalance in regional oxygen supply and demand

Keeping the rSO2 levels at 75% or greater of the preinduction values was associated with a decreased length of stay in hospital.

- Increasing perfusion pressure
- Pump flow
- PaCO2 > 35 mmHg
- Decreasing temperature < 37°C
- Increasing Ht > 20%

Murkin JM, Seminars in Cardiothor Vasc Anesth. 2004;1:13
NIRS

• rSO2 <41% during CABG was associated with frontal lobe dysfunction


• rSO2 <50% or a relative decrease of more than 20% from baseline values were associated with reduction in amplitude of AEP, indicative of focal cerebral ischemia

Normal NIRS during CPB

- ↓ rSO2 < 25% (Murkin)
- rSO2 > 41% (Edmonds)
- rSO2 > 50% (Cho)
Abnormal NIRS during CPB

- \( \downarrow \text{rSO}_2 > 25\% \) (Murkin)
- \( \text{rSO}_2 < 41\% \) (Edmonds)
- \( \text{rSO}_2 < 50\% \) (Cho)
NIRS and TEE in aortic dissection

Locatelli A MD
rSO2%

False lumen cannulation → start ECC

Locatelli A MD
NIRS

rSO2%

Stop ECC

Locatelli A MD
TEE (true lumen cannulation)
NIRS

Restart ECC

True lumen cannulation
NIRS in selective cerebral perfusion

Open distal anastomosis

T. Kazui
Arch-vessels cannulation
Axillary perfusion
En block technique

Four-Branched Aortic Arch Graft
Separate graft technique
NIRS in SCP *en block* technique

A- Induction
B- ECC
C- 25° C
D- Arch-vessels cannulation
E- SCP
F- Final anastomosis arch-vessels
G- restart ECC
H- stop ECC
NIRS advantages

- Noninvasive, continuous

- Correlate with conventional measures of global brain metabolism

- Useful even in absence of flow

References:

Kurth CD et al. Anesthesiology. 1995;82:74
NIRS limitations

- Inability to distinguish between intra- and extracranial changes in blood flow and oxygenation

- Extracranial contamination affects the reliability of the readings.

TRANSCRANIAL DOPPLER ULTRASONOGRAPHY (TCD)

TCD measures velocity in the proximal segment of the middle cerebral artery (MCA)

MCA provides 70% of the blood flow to the ipsilateral cerebral hemisphere
TCD

- There is a significant correlation relative changes in cerebral blood flow (using Xe$^{133}$ Clearance) and changes in MCA velocity


- Detection of cerebral microembolization (emboli quantification is achieved by appropriate discrimination between the lower intensity flow velocity spectrum and emboliform "high-intensity transient signals" -HITS-)

NORMOCAPNIC

Pulsatility index = \( \frac{V_{\text{max}} - V_{\text{min}}}{V_{\text{mean}}} \)

0.94
Pulsatility index = \frac{(V_{\text{max}} - V_{\text{min}})}{V_{\text{mean}}}

0.61
IPOCAPNIC

Pulsatility index\(=\frac{V_{max}-V_{min}}{V_{mean}}\)

2.24
Autoregulation

Cerebral Flow \( (V_{\text{max}}) \) k for 50-150 mmHg Arterial pressure range

Mean arterial pressure 85 mmHg

Mean arterial pressure 70 mmHg
Cross-clamp release
Side clamp release (OPCABG)
**TCD**

Association between no. of emboli detected intraoperatively and neurobehavorial outcome

<table>
<thead>
<tr>
<th>Microemboli count during deficit CPB</th>
<th>No. pts</th>
<th>No. with deficits</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td>58</td>
<td>5</td>
<td>9 %</td>
</tr>
<tr>
<td>201-500</td>
<td>13</td>
<td>3</td>
<td>23%</td>
</tr>
<tr>
<td>501-1000</td>
<td>16</td>
<td>5</td>
<td>31%</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>7</td>
<td>3</td>
<td>43%</td>
</tr>
</tbody>
</table>

Stump DA in Tegeler CH (eds). Mosby-Year Book 1999
• The presence of >50 microembolic signals/hour during the early postoperative phase is reported to predict the development of focal cerebral ischemia


• Infusion of antiplatelet agent in patient with more than 25 HITS in 10 minutes, reduced postoperative stroke rate in CEA, from 3% to 0%

TCD advantages

- Noninvasive, continuous monitor of cerebral perfusion
- Can detect clinically significant microembolization
- Can detect instantaneous changes in CBF (important in carotid artery surgery, procedures involving selective antegrade or retrograde cerebral perfusion, and repair of congenital cardiac defects in neonates)

Ringelstein EB et al. Stroke. 1998;29:725
TCD limitations

- 10% of patients cannot be assessed through the temporal window
- Operator dependent
- Difficulty of reproducibility especially at low flow
- Absent signal during low flow and DHCA

EEG

- Represents spontaneous electrical activity of the cerebral cortex and is generated mainly by summation of excitatory and inhibitory post-synaptic potentials of cortical neurones.

- It does not reflect activity in subcortical levels, cranial nerves or the spinal cord.

The electrical signal is amplified, filtered and then displayed as either 8 or 16 channels (eight channels per hemisphere) to give an accurate representation of electrical activity throughout the cortex.

**EEG parameters**

- Frequency
- Amplitude

**EEG**
<table>
<thead>
<tr>
<th>Activity</th>
<th>Frequency</th>
<th>Physiology</th>
<th>Pathology</th>
<th>Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>δ</td>
<td>&lt;4 Hz</td>
<td>Normally seen in deep sleep (slow wave sleep)</td>
<td>Ischaemia, drug overdose, metabolic derangements</td>
<td>Deep anaesthesia</td>
</tr>
<tr>
<td>θ</td>
<td>4-8 Hz</td>
<td>Normally present during drowsiness</td>
<td>Ischaemia, drug overdose, metabolic derangements</td>
<td>Common during general anaesthesia</td>
</tr>
<tr>
<td>α</td>
<td>8-13 Hz</td>
<td>Dominant in the occipital cortex, during alert wakefulness with eyes closed</td>
<td>Light anaesthesia</td>
<td></td>
</tr>
<tr>
<td>β</td>
<td>&gt;13 Hz</td>
<td>Common in alert patients with eyes open</td>
<td>Light anaesthesia, small doses of benzodiazepines and barbiturates</td>
<td></td>
</tr>
</tbody>
</table>


- Oligoaaemia
  - $\downarrow pHi = PCr$
  - $\uparrow O_2 \text{ ER} = ATP$

- Functional threshold
  - $\downarrow pHi$
  - $\downarrow PCr$
  - $\uparrow O_2 \text{ ER}$
  - $\downarrow ATP$

- Lesion threshold
  - $\downarrow pHi$
  - $\downarrow PCr$
  - $\uparrow O_2 \text{ ER}$
  - $\downarrow ATP$

- CBF ml/100 gr/min

- 50
- 20
- 10

- Time
  - 30 min
  - 120 min
  - 6 h
  - 24 h
<table>
<thead>
<tr>
<th>Condition</th>
<th>CBF Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean normal CBF</td>
<td>50 ml/100 gr/min</td>
</tr>
<tr>
<td>Mild hypoperfusion well tolerated, not induce neuronal dysfunction</td>
<td>up to 22 ml/100 gr/min</td>
</tr>
<tr>
<td>Decrease in EEG amplitude and/or EEG slowing</td>
<td>below 22ml/100 gr/min</td>
</tr>
<tr>
<td>Flattening EEG</td>
<td>7-15 ml/100 gr/min</td>
</tr>
</tbody>
</table>

Grady RE et al. Anesthesiology. 1998;88:892
A progressive reduction of CBF produces:

- Decrease in fast activity (decrease of $\alpha$ and $\beta$)
- Decrease in amplitude
- Appearance of $\delta$ rhythms
A severe brain hypoperfusion is characterized by:

- Disappearance of $\alpha$ and $\beta$ and a predominance of $\delta$ frequencies

- 75% attenuation of all activities and/or a more than 100% increase of $\delta$ activities slower than 1 Hz
The amplitude of $\alpha$ and $\beta$ frequency bands are the most relevant follow-up criteria for hypoperfusion induced by a drop in blood pressure during ECC.

**Prior PF. Electroencephalogr Clin Neurophysiol. 1987;39S:221**

- **Criteria for severe hypoperfusion:**
  More than 30% amplitude decrease for more than 30 s.

Most anaesthetics agents cause similar EEG changes:

• first the disappearance of the $\alpha$ rhythm and the appearance of $\beta$ activity,
• then a progressive slowing toward $\theta$ and $\delta$ rhythm

At subanaesthetic doses, anaesthetic drugs induce EEG activation. Deep anaesthesia is associated with burst suppression pattern or electrical silence.
Analogic EEG Raw data

Need for post-processing
To facilitate interpretation of the standard raw EEG, different EEG processing method have been developed:

- Periodic analysis (Cerebral function monitor; Klein analyzator)
- Aperiodic analysis (Lifescan)
- **Power spectral analysis** (Compressed Spectral Array; Density Modulated Spectral Array)
The most common processing techniques used is Power Spectral Analysis through the **Fast Fourier Transform (FFT)**.

FFT is a method to decompose the signals into sine waves, and this analysis results in the power spectrum of the EEG.
Data obtained with FFT are presented under the form of Compressed Spectral Array (CSA).

CSA consist in determining the power-frequency curve for a given time period (Epoch) and to present successive time periods in a same display.

CSA is graphical representation of analogue EEG

The principles of visual interpretation are similar to these used in raw EEG:

• Identification of an overall power decrease (attenuation)

• Power increase of $\delta$ and $\theta$ frequency bands (slowing)


Quantitative frequency variables extracted from the spectra:

**SEF 95 (Spectral Edge Frequency):** the frequency under which the 95% of the global power is contained

**MPF (Median Power Frequency):** the frequency under which the 50% of the global power is contained

**MDF (Main Dominant Frequency):** mean frequency in the 8-15 Hz frequency band

Bashein G et al. Anesthesiology. 1992;76:878
Quantitative power variables extracted from the spectra:

**TP (Total Power):** the sum of the power of any frequency

**Relative power band:** for a given frequency band ($\alpha, \beta, \delta, \theta$) the ratio between the power of this band and the total power (e.g., $\theta + \delta / \alpha + \beta$)

*Sainio K et al. Electroencephalogr Clin Neurophysiol. 1983;556:117*
EEG patterns correlate with CBF

Hypoxaemia initially produces an acute increase in amplitude of the EEG, followed by a reduction in amplitude and the appearance of slow waves, but this may be masked by deep anaesthesia.

Persistent EEG changes may predict neurological deficit.
Brain oligaemia occurs when:

- **50% decrease of graphical SEF**

- **Graphical SEF <7 Hz**

- **50% bilateral decrease of Total Power or bilateral increase of relative δ and θ power**
EEG

Brain hypoperfusion:

• **Decrease** in Total power, **decrease** in relative α and β power with an **increase** in relative δ and θ power


• **Loss of symmetry**

EEG monitoring

Pre-induction
\[
\frac{\alpha}{\delta} = 1.38 \\
\delta + \theta / \alpha + \beta = 0.72
\]
Steady-state
Failed weaning from CPB

↓ TP 50%
SEF from 9 to 3 Hz
\[ \alpha / \delta = 0.037 \]

\[ \delta + \theta / \alpha + \beta = 15.2 \]
Successful weaning from CPB
EEG monitoring

“Burst” suppression

[Diagram showing EEG monitoring with specific time markers and frequency ranges]
Propofol 200 mg ev
DHCA TC 16° C
EEG advantages

• Noninvasive, continuous
• Good correlation with changes in CBF
• Online monitor, allows rapid intervention

EEG limitations

- Experienced personnel
- Artifact or electrical noise
- Lack of sensitivity to detect subcortical
- Influenced by anesthetic

Bashein G et al. Anesthesiology 1992;76:878
High-resolution color Doppler imaging allows visualization of the central retinal artery and measurement of its blood flow velocity, which reflects internal carotid artery flow. A reduced retinal artery flow reflects cerebral hypoperfusion.
S-100 protein is composed of 2 subunits: S-100α, (heart, striated muscle, and kidney); S-100αβ (glial cells); and S-100ββ (astrocytes and Schwann cells). With neurologic injury accompanied by increased blood-brain barrier permeability, S-100β leaks from damaged nerve cells into the peripheral blood and cerebrospinal fluid and thus may serve as an index of central nervous system damage.

After acute ischemic stroke, peak levels of S-100 occur 3 days after the insult; whereas during cardiac surgery, peak values occur soon after reperfusion.

The early release of S-100 after cardiac operations is transient and may reflect increased blood-brain barrier permeability as part of the systemic inflammatory response and elevated levels because of extracerebral S-100 sources like cardiotomy suction and shed mediastinal blood.

• Detects preexisting neurologic deficit
• Correlates with perioperative neurologic injury

S 100 limitations

- Possible contamination from extraglial sources
- Multiple sampling periods required
- Not a bedside patient test
Xenon washout technics

The diffusible radioactive tracer ($^{133}$Xe) is administrated and the rate at which radioactivity disappears from the head can be monitored using external detectors, which are placed in various position over the skull and detect photons. The radioactivity washout curve slope is proportional to the regional CBF.

Obrist WD et al. Cerebrovascular Brain Metabolism Review. 1990;2:283
Conclusions

Probably, there is no “ideal monitor”, and the use of more than one (so-called “multimodality monitoring”) may be required.

These neuromonitoring methods used routinely can improve overall patient outcome and reduce hospital length of stay.
Questions

- Need for guidelines
- Need for adequate training
- Anesthesiologist as coordinator between surgeons and perfusion technicians
- Need for clinic neurophysiologist in operating room?