State of the Art Anesthetic Approaches to Improve Perioperative Neurologic Outcomes

Jeffrey R. Kirsch, MD FASA
(kirschje@ohsu.edu)
Oregon Health & Science University

Disclosures

- Experience
  - Bench research from 1976 to 2005 (NIH funding from 1987 to 2005) to understand the mechanisms of brain injury following hypoxia/ischemia
  - Busy clinician; Member ASA Periop Brain Health Commit
- Financial
  - I do not accept honoraria for lectures, book royalties, legal case reviews or consulting. All fees are paid to a charity. Most commonly to FAER, Oregon Food Bank

Objectives (protecting brain)

- Participants should be able to
  - Describe the limited utility of GA for protection of the human brain from injury or cerebral ischemia (cardiac arrest, temporary clipping during cerebral aneurysm clipping).
  - Develop clinical strategies to minimize the occurrence of post-operative delirium in high risk patients.
  - Develop an evidence-based anesthetic plan for cerebral clot retrieval
  - Develop Anesthetic plan for management of patients having spine surgery
How can it be?

• In the 1980s (and still some believe today): General Anesthetics are Neuro-protectors
• In 2010: General Anesthetics are found to be Neuro-toxic!

Lecture Topics

• Anesthetics as neuro-protectants in the setting of cerebral ischemia
• Effect of Anesthetics on patients during cerebral clot retrieval
• Effect of Anesthesia/Surgery on Postoperative neurologic function (delirium)
• Supporting optimal neurologic recovery following spine surgery

Good news and bad news

• Good news if you are a rodent
  – Many studies demonstrate approximately 30% reduced injury from focal ischemia by most of the anesthetics
• Bad news if you are a human
  – No anesthetic agent has been demonstrated to be protective to the human brain
43 y.o. mother of three with multiple cerebral cerebral aneurysms

- As the surgeons approach the aneurysm they indicate that they are going to use a temporary clip and ask you to institute “brain protection”. What are going to do?
  A. Propofol?
  A. To what end-point?
  B. Desflurane?
  C. Hypothermia?
  D. Hypertension?
  E. Ketamine?

Preventing injury from cerebral ischemia

- Monitoring for ischemia: Neurologic exam, EEG, SEPs, Near Infrared spectroscopy
  Jugular bulb oxygen saturation, paratrend, micro-dialysis
- Facilitating perfusion: BP control
  (particularly in a non-autoregulating vascular bed)
- Avoiding unnecessary hyperventilation
- Avoiding hyperthermia
- Avoiding hyperglycemia and hypoglycemia

Mechanistic treatment to prevent brain injury from cerebral ischemia

Mechanistic treatment only effective in rodents

- Protease inhibitors
- Anti-inflammatory/adhesion agents
**Hypothermia bad during focal ischemia in humans**

Mortality by 90 days (%):
- Hypothermia: 21.4%
- Nonhypothermia: 16.7%
- p = 0.746

SAE indicates serious adverse event. ICX, intracranial hemorrhage.

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**TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA**

*NEJM 346, 2002*

<table>
<thead>
<tr>
<th>Hypothermia</th>
<th>Nonhypothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td>137</td>
<td>130</td>
</tr>
<tr>
<td>95</td>
<td>94</td>
</tr>
<tr>
<td>83</td>
<td>83</td>
</tr>
<tr>
<td>11</td>
<td>9</td>
</tr>
</tbody>
</table>

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**Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest**


<table>
<thead>
<tr>
<th>Outcome</th>
<th>33°C Group</th>
<th>36°C Group</th>
<th>Hazard Ratio or Risk Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcomes: deaths at end of trial</td>
<td>215/473 (46)</td>
<td>227/468 (48)</td>
<td>1.06 (0.84-1.34)</td>
<td>0.51</td>
</tr>
<tr>
<td>Secondary outcomes: Neurologic function at follow-up</td>
<td>116/256 (46)</td>
<td>122/252 (48)</td>
<td>1.02 (0.84-1.26)</td>
<td>0.78</td>
</tr>
<tr>
<td>Modified Rankin scale score of 4-6</td>
<td>245/480 (51)</td>
<td>253/468 (54)</td>
<td>1.01 (0.84-1.20)</td>
<td>0.92</td>
</tr>
<tr>
<td>Deaths at 30 days</td>
<td>226/473 (48)</td>
<td>232/468 (47)</td>
<td>1.08 (0.87-1.35)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

*The hazard ratio is shown for the primary outcome, and odds ratios are shown for the secondary outcomes. CI denotes confidence interval.*

*The neurologic follow-up was specified in the protocol to be performed at 30 days, but the time to follow-up was not consistent across centers. The modified Rankin Scale was used to assess neurologic outcome.*

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Risks of Hypothermia

- Increased incidence of morbid cardiac events (Frank et al., JAMA 277:1127, 1997)
- Coagulopathy (Staab et al., J Trauma 36:634, 1994), not due to hypothermia-induced platelet dysfunction (Faraday, Anesthesiology 88, 1579, 1998)
- WBC dysfunction and decreased number (Akrion J Leukocy Biol 37:51, 1985)
- RBC sludging
- Poor release of oxygen from RBC.

Hypothermia is no longer indicated as a treatment to prevent post-ischemic neurologic injury (Except if you are taking the 2015 ACLS recertification examination)

Desflurane prevents ischemia-induced acidosis in humans (improved collateral flow?)

Hoffman WE Anesthesiology 88:1188, 1998

Should desflurane or etomidate/propofol be used for burst suppression during aneurysm or CEA surgery?
Problems with high dose Desflurane

Cost
Prevents neuromonitoring

Nitrous Oxide

- Decreases efficacy of Barbiturates as a neuroprotectant (Warner et al., Anesthesiology 73:686, 1990)
- Decreases efficacy of isoflurane as a neuroprotectant (Baughman et al., Anesthesiology 70:767, 1989)
- May worsen outcome because of an increase in CMRO2
- Alone provides inadequate anesthesia
- high catecholamine concentration may contribute to worse outcome
- Increases transient neurologic deficits in humans exposed to temporary clipping for aneurysm surgery (Pasternak JJ et al., Anesthesiology 110: 563, 2009)

Do Not administer N2O in patients at risk for cerebral ischemia

Alpha-2 Adrenergic Agonists

- Selective attenuation of ischemia-induced increases in striatal norepinephrine release (Matsumoto et al., Brain Res 627:325, 1993)
- However, Alpha-2 agonists may prevent hyperemia and appropriate oxygen supply during hypoxia (McPherson, Anes Anal 84:139, 1997) because of direct pial vasoconstriction (Iida Anesthesiology 91:479, 1999), which may exacerbate ischemic injury (Nakano T J Anesth 23:378, 2009)
- Decreases neuro-inflammation (Jiang L et al., J Clin Anesth. 40:25, 2017)
- Does not increase the need for intra-carotid shunting during CEA, but effect on cognitive function not assessed (Bekker et al., Anes Anal 103:955, 2006)

Alpha 2 agonists do not protect human brain from ischemia induced injury. May prevent post-op delirium following deep GA.
Brain protection: what are going to do?


B. Desflurane? Maybe (Hoffman et al), but impairs ability to monitor MEPs.

C. Hypothermia? No!

D. Hypertension? Good to try when monitoring suggests ischemia.

E. Ketamine? 0.5 mg/kg IBW; Hudetz et al, at least for CP bypass.

65 year old man with Right MCA occlusion

- History of atrial fibrillation on aspirin treatment.
- PMH: Hypertension, Type 2 diabetes, high cholesterol, inactive.
- PE: BMI 32, MP 3 airway, NPO for 6 hours after a light meal.
- Interventional radiologist wants to proceed with clot retrieval.

Additional preoperative assessment?

- GA vs Sedation?
- Specific plans for neuroprotection?
Retrospective studies cannot exclude the likelihood that sicker patients were chosen for GA and no study was controlled to address differences in blood pressure or PaCO2.
Anesthesia for Clot Retrieval

- Consider sedation rather than GA
- Avoid hyperventilation
- Avoid hypotension
- Consider low dose (0.5 mg/kg; single dose) ketamine
- If GA: Desflurane for anesthetic maintenance
### Good news and bad news

- **Bad news for rodents**
  - Many studies demonstrate neurotoxicity of IV and inhaled anesthetics at extremes of age
- **“Good news” if you are a human**
  - Sub-human primate data require either long duration of anesthetic or at least 3 repeat exposures in fetus/newborns (Brambrink).
  - MASK Trial (Anesth 2018:129:89): Multiple exposures before age 3 required to cause limited learning difficulties
  - Retrospective analysis of older adults (BJA 2018:121:398) demonstrates small acceleration of cognitive decline following surgery/anesthesia

### How did we miss the fact that anesthesia/surgery is associated with post-operative delirium?

**Is Anesthesia-induced POCD a reality?**

### Is neurologic injury associated with perioperative care? If so:

- What are the clinical markers of perioperative neurologic injury (e.g. Stroke, delirium, cognitive dysfunction)?
- Is the frequency of injury worse with particular surgical interventions?
- What are the patient factors that cause higher risk of neurologic injury during the perioperative period (e.g. age, gender, co-morbidities, frailty index)?
Why try to prevent POD?

• May evolve to Postoperative Cognitive Dysfunction (yes, at 1 month, but not at 1 year)
• Patient may physically hurt themselves
  – Self-extubation
  – Pull out invasive lines
  – Disrupt nutrition or medication administration
• Patient may physically hurt a health care provider

Should a discussion about POD be included in our PARQ discussions?

A. No, because it is so rare?
B. Yes, in all patients?
C. Yes, but only in patients at the extremes of age (i.e. very young and very old)?
D. Yes, but only in patients with pre-existing dementia?

Table 1: Incidence of delirium in most series

<table>
<thead>
<tr>
<th>Surgery type</th>
<th>Study</th>
<th>Population</th>
<th>Delirium rate (%)</th>
<th>Selection method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrelated</td>
<td>Krieter et al.</td>
<td>Recovery room after elective general anesthesia</td>
<td>16.9</td>
<td>No DESC</td>
</tr>
<tr>
<td>Surgical ICU</td>
<td>Necker et al.</td>
<td>Surgical ICU</td>
<td>10</td>
<td>Not stated</td>
</tr>
<tr>
<td>Head and neck</td>
<td>Weid et al.</td>
<td>Major head and neck</td>
<td>1.7</td>
<td>Not stated</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Komaromi et al.</td>
<td>Cardiac surgery with CPB</td>
<td>14.3</td>
<td>DSM-IV</td>
</tr>
<tr>
<td></td>
<td>Topchid et al.</td>
<td>Patients who undergoing elective or urgent cardiac surgery</td>
<td>4.7</td>
<td>DSM-IV</td>
</tr>
<tr>
<td></td>
<td>Sutmirski et al.</td>
<td>Patients who undergoing elective coronary artery bypass grafting or valve replacement</td>
<td>48</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>Vascular</td>
<td>Wroclawski et al.</td>
<td>Abdominal aortic aneurysm repair</td>
<td>38-64</td>
<td>DSM-IV</td>
</tr>
<tr>
<td></td>
<td>Schrader et al.</td>
<td>Bronchial aorta</td>
<td>17.5</td>
<td>DSM-IV</td>
</tr>
<tr>
<td></td>
<td>Strother et al.</td>
<td>Thoracic surgery</td>
<td>15-43</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>Fisher and Fleisher</td>
<td>Patients with undergoing elective orthopaedic procedure</td>
<td>25-41</td>
<td>DSM-IV</td>
</tr>
<tr>
<td></td>
<td>Wroclawski et al. and Lee et al.</td>
<td>Patients with undergoing emergent hip fracture repair</td>
<td>16.2-41</td>
<td>DSM-IV</td>
</tr>
</tbody>
</table>
Patients developing delirium were older, more often female, had lower pre-op cognitive scores and underwent longer operations. Neither degree or duration of hypotension were significantly associated with post-op delirium. Rather, intra-op BP variance was significantly associated with post-op delirium.

Postoperative Brain Dysfunction is more common:

- In elderly patients having major surgery
- In women
- In patients with pre-existing brain dysfunction/cerebrovascular disease
- Following on-pump cardiac surgery with an arrested heart or deep hypothermia
- Following heart surgery when more vasopressors are needed and there is more BP variability

Are there modalities that we can monitor and act upon to minimize the risk of postoperative delirium?
Is there scientific evidence for the “within 20% of baseline” blood pressure goal to prevent postoperative neurologic dysfunction?

“Only low-level evidences links low rScO2 during cardiac surgery to postoperative neurologic complications, and data are insufficient to conclude the interventions to improve rScO2 desaturation prevent stroke or POCD”

CONCLUSIONS: Intraoperative hypotension might play a role in the development of postoperative ischemic stroke. Especially for mean blood pressure values decreasing more than 30% from baseline blood pressure, an association with postoperative ischemic stroke risks was observed.
Facilitation of cerebral perfusion by maintaining optimal blood pressure is an important strategy to prevent postoperative brain dysfunction.

Post-op delirium (POD) and cognitive dysfunction (POCD) has been elucidated on the molecular basis and many biomarkers have been identified. However, little has been proven regarding cause and effect.
IS INFLAMMATION AN IMPORTANT MEDIATOR OF POD?

KETAMINE

(Anti-Anweseh, Belg, 2012: 42-52)

The anti-inflammatory effects of ketamine: state of the art
S. Loox (*), M. De Kock (**), and P. Hosty (*)
At low doses Ketamine:

- Inhibits NMDA-receptor activation
- Mediates beneficial changes in apoptosis-regulating proteins
- Interferes with the inflammatory response to injury (neither low or high dose steroids protect the brain).
- Cardiovascular stimulation may improve cerebral perfusion

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Ketamine Attenuates Delirium After Cardiac Surgery With Cardiopulmonary Bypass

Judith A. Hudetz, PhD, Kathleen M. Farkas, PhD, Zafar Ismail, MD, Santwe D. Garelli, MD, Allison J. Byrne, PhD, Anthony G. Hudetz, DVM, PhD, David C. Whalley, MD, PhD, and Paul S. Fegley, MD, PhD

Objective: To determine if ketamine attenuates postoperative delirium in patients undergoing cardiac surgery with cardiopulmonary bypass.

Methods: A prospective, randomized, double-blind study.

Setting: A Veterans Affairs medical center.

Patient Selection: Patients at least 18 years of age randomly received placebo (0.9% saline, n = 26) or an intravenous ketamine (0.5 mg/kg intravenously, n = 26) during neuromuscular blockade in the presence of ketamine and nitrous oxide.

Primary Outcome: The incidence of postoperative delirium was lower (p = 0.01) in patients receiving ketamine (0%) compared with placebo (31%). Postoperative cognitive performance was also better (p = 0.008) in the ketamine group compared with placebo.

Secondary Outcomes: The odds of developing postoperative delirium were greater for patients receiving placebo compared with ketamine/midazolam (odds ratio = 0.36, 95% confidence interval).

Conclusion: After cardiac surgery using cardiopulmonary bypass, ketamine attenuates postoperative delirium.
DEXMEDETOMIDINE

The effects of dexmedetomidine on post-operative cognitive dysfunction and inflammatory factors in senile patients
Wen Jin Chen, Bo Liu, Peng Zhang, Feng Xiao, Rongping Cui, Weifu Lei

Table 1. MMSE and incidence of POCD

<table>
<thead>
<tr>
<th>Cases</th>
<th>MMSE</th>
<th>POCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>(n)</td>
<td>Before</td>
</tr>
<tr>
<td>Size</td>
<td>(n, %)</td>
<td>Surgery</td>
</tr>
<tr>
<td>Dex group</td>
<td>87</td>
<td>26.24 ± 5.18°</td>
</tr>
<tr>
<td>Control group</td>
<td>61</td>
<td>26.51 ± 5.42°</td>
</tr>
</tbody>
</table>

P < 0.05 vs before surgery; *P < 0.05 vs control group; **P < 0.01 vs control group.

Table 2. Levels of IL-6 and TNF-α before and after surgery

<table>
<thead>
<tr>
<th>Cases</th>
<th>IL-6 (pg/mL)</th>
<th>TNF-α (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Size</td>
<td>Surgery</td>
<td>Surgery</td>
</tr>
<tr>
<td>Dex group</td>
<td>87</td>
<td>49.41 ± 9.53°</td>
</tr>
<tr>
<td>Control group</td>
<td>61</td>
<td>51.02 ± 30.49</td>
</tr>
</tbody>
</table>

*P < 0.05 vs before surgery; **P < 0.05 vs control group; ***P < 0.001 vs control group.

Dexmedetomidine for prevention of delirium in elderly patients after non-cardiac surgery: a randomised, double-blind, placebo-controlled trial
Lancet 2016; 388: 1893-902

![Graph showing comparison of dexmedetomidine and placebo groups]
1. 3 year survival improved by dex in non-cancer pts
2. Cognitive function is improved by dex for all 3 year survivors
3. 2 year survival was improved by dex in all pts

“Unlike its use as a sedative in the intensive care unit, intraoperative dexmedetomidine did not significantly reduce the incidence of delirium over saline placebo (12.2% vs 11.4%).” ... “This result may be due to the short-acting nature of the drug and loss of salutary effects after discontinuation of the infusion.”
Post-op mini-mental scores in lidocaine treated patients were better and associated with suppressed release of IL-6, S100B and NSE at the end of surgery and 3 days post-op.

How many times have you walked into a room to find high concentrations of inhaled agent being administered and phenylephrine/norepinephrine being infused in order to provide “adequate anesthesia” in an elderly person?
Maintaining BIS between 40 and 60 (in adults) during surgery may result in reduced incidence of post-operative delirium

Is Xenon the “miracle” drug to prevent post-op neurocognitive dysfunction? NO
Interventions for preventing delirium in hospitalised non-ICU patients.

**Authors’ conclusions**
- Using the Bispectral Index to monitor and control depth of anaesthesia reduces the incidence of postoperative delirium. The role of drugs and other anaesthetic techniques to prevent delirium remains uncertain.

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**Postoperative Brain Dysfunction (e.g. delirium) is common**
- In elderly patients having major surgery (up to 50% following cardiac surgery)
- In women
- In patients with APOE ε4 allele
- In patients with pre-existing brain dysfunction/cerebrovascular disease
- Following on-pump cardiac surgery with an arrested heart or deep hypothermia
- Following heart surgery when more vasopressors are needed and there is more BP variability
- In patients with BIS below 40 during surgery

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**Reduced risk of post-operative delirium**
- BIS 40-60 during surgery
- MABP 80; ideally within 10% of baseline
- Consider IV Lidocaine (1.5 mg/kg/hr; max 30 mg/hr)
- Consider IV Ketamine 0.5 mg/kg (Single dose)?
- Consider IV dexametomidine infusion (1 mcg/kg over 10 min at the end of the case, post-operative or intra-nasal)
Spine Surgery

- Potential Clinical Scenarios
  - Acute spine trauma
  - Spine deformity
  - Back Pain
- Preventing injury during intubation
- Control of perfusion
- Neuromonitoring
- Timely emergence risks to improve care for the patient and make your surgeon

21 year old football player suffers incomplete cervical spine injury during a game
Patient Care/Treatment Issues

- Steroids: AANS, Congress of NS, EM all indicate glucocorticoids is a treatment option, not treatment standard
- Surgery: Goal neural element decompression and stabilization, but no guidelines. Generally agreed that early surgery (before 24 hours) is associated with improved outcomes following incomplete injury
- Experimental treatments: None are recommended (e.g. cooling, electrical stimulation, GM-1 etc)

Anesthesiology Issues

- Airway management
- CV: Spinal shock; Autonomic hyper-reflexia, impact on myocardial function
- Impact on temperature control
- CV and Neuro Monitoring suggestions
- Positioning on frame
  - Lungs; CV; Eyes
- Preventing delayed emergence
1. DL produces extension (MAC>Miller)
2. FM/Chin lift produces as much neck movement as DL
3. Video and flexible scopes produce the least cervical movement
4. ILMA and lighted stylets associated with less C1/C2 & C2/C3 movement than DL
5. Some avoid (forceful) cricoid pressure because of associated cervical movement
6. Flexible scope safe, except risk of coughing during awake intubation

Airway Management

Choices

• Awake vs RSI (surg airway backup) vs Awake trach?
• DL vs Video laryngoscopy vs flexible (Emergent vs. Elective)
• If awake: airway blocks or not?
• If RSI: In-line stabilization or leave collar in place?
• Cricoid pressure or not?
• Sux before 48 hrs or not? Roc with sugammadex?
• Pretreatment with glycopyrolate or not?
• Etomidate, Ketamine or Propofol?
• Early initiation of vasopressor infusion?
Acute Responses (0-6 weeks)
- Hemodynamic alteration
- Hypotension, tachycardia
- Spinal shock
- Hypotension + IOM, bradycardia
- Bradycardia, bradycardia arrhythmias, AHR block, cardiac arrest

Potential Triggers
1. Bowel
2. Bladder
3. “Pain”
4. Sexual Stimulation
5. Skin sores

Signs/symptoms
1. HTN
2. Headache
3. Flushed face
4. Sweating above spinal level
5. Nasal stuffiness
6. Bradycardia
7. Nausea
8. Cold/clammy below level

Pathophysiology:
- Autonomic hyper-reflexia

Cardiovascular Monitoring
- Standard monitors
- Invasive BP with PPV
- Urine output
- +/- central access often require vasoactive infusion
- Monitoring for spinal shock, Autonomic hyper-reflexia, prone position

(Manogue et al., Heart Rhythm 2017; 14:920)
Postoperative Visual Loss/Injury (0.05% to 1%)

- Corneal abrasion
- Ischemic optic neuropathy: Inc IOP causing optic nerve damage
- Central retinal artery occlusion: vasospasm, emboli, compression or hypotension
- Cortical blindness: ischemia

Eye Injury Prevention

- Frame with a mirror to monitor for compression, open lid etc.
- Slight 10% reverse Trendelenburg
- “Tight control” of blood pressure (MABP>70), Hct>30%
Blood Pressure Augmentation

Augmentation of systemic blood pressure during spinal cord ischemia to prevent postoperative paraplegia after aortic surgery in a rabbit model

- Rabbit late paraplegia model involving infrarenal aortic occlusion for 15 minutes

- HBP group, n=8
  - MAP 120 mm Hg
  - IV phenylephrine

- LBP group, n=8
  - MAP 50 mm Hg
  - IV nitroprusside

- Control, n=8
  - MAP 80 mm Hg

- All 48 hours; 100% HBP group did not have paraplegia

BP Management

- American Association of Neurologic Surgeons recommends (based on retrospective studies)
  - MABP 85 to 90
  - SBP no lower than 90
  - Minimize duration of hypotension

- BP treated with IV fluid/blood for PPV greater than 11 to 13

- Preference for norepinephrine as compared to phenylephrine

- No data exists to guide intraoperative use
Study Design

- Multi-centric Randomized Controlled Trial funded by Department of Defense (PI Miriam Treggiari MD, PHD)

- 152 participants with high spinal cord injury

- 2 concurrent groups with different MAP targets
  - Augmentation group: induced blood pressure with a MAP goal of 85-90 mm Hg
  - Conventional group: conventional blood pressure with a MAP goal of 65-70 mm Hg
Neuromonitoring
(Hadley et al., Neurosurgery 81:713, 2017)

- Multimodality intraoperative monitoring, including SSEPs and MEPs, during spinal cord/spinal column surgery is a reliable and valid diagnostic adjunct to assess spinal cord integrity and is recommended if utilized for this purpose.
- MEP recordings are superior to SSEP recordings during spinal cord/spinal column surgery as diagnostic adjuncts for assessment of spinal cord integrity and are recommended if utilized for this purpose.

General Principle of IONM

Communication!
- neurophysiologist
- Anesthesiologist
- Surgeon
- Documentation

Somatosensory Evoked Potentials
- SEP recording has become a standard method in intraoperative monitoring during spine surgery.
- It is based on a close relationship between spinal blood flow and SEP changes.
- SEPs are sensitive to local factors such as
  - Pressure,
  - Heat,
  - Systemic parameters like blood pressure, body temperature, and metabolic changes.
Anesthesia

- The major target of anesthetic action appears to be synaptic function
- The net effect of anesthetic agents:
  1. Depression of the synaptic function
     - Decrease the amplitude
     - Increase cortical excitability
  2. Alteration of synaptic function of secondary neural pathways, cause additional depression
  3. State of unconsciousness and lack of movement
     - Alter spinal reflex activity and motor EPs
     - Block sensory information at the thalamus
Recommended Anesthetic Regimen for SSEP

- Continuous infusion of opioid (or dexmedetomidine) + Infusion of propofol with or without low dose isoflurane (0.5–1.0%) or sevoflurane (0.8–1.7%) in O2/air
- Muscle relaxants as required (omit if EMG or MEPs monitored)

Recommended Anesthetic Regimen for MEP

- Continuous infusion of opioid (or dexmedetomidine) + infusion of propofol
- Avoid inhaled anesthetics, as appropriate
- Avoid all muscle relaxants * during period of monitoring
- (lidocaine (1.5 mg/kg/hr; max 30 mg/hr) infusion may be a useful adjunct)

Strategies for rapid emergence from a propofol based anesthetic

- BIS/EEG Monitoring (don’t forget extra propofol syringe in-line)
- Balanced with other short-acting agent (e.g. Dex, Remi, Sufenta)
- Esmolol bolus (500 mcg/kg 10 min prior to induction) plus infusion (200 mcg/kg/min) using BIS (Asouhidou I et al BMC Anesthesiol 2015:15:172)
Lecture Goals

• Is surgery/anesthesia associated with post-op brain dysfunction (delirium/POCD/Stroke)?
  – Yes, particularly in elderly who have pre-existing evidence of cognitive dysfunction, under deep anesthesia (low BIS) with low or variable BP requiring vasopressor resuscitation.

• Do anesthetics protect the brain from injury in the setting of focal cerebral ischemia?
  – Maybe ketamine (anti-inflammatory), kappa agonists and desflurane (blood flow promotion). Propofol is not helpful and N2O is dangerous.
  – No outcome difference following clot retrieval for GA vs. MAC

• Can anesthetic management impact outcomes following spinal cord injury?
  – Yes, airway management to maintain structural integrity; BP control to impact perfusion; anesthetic choices to allow intra & postoperative neuro-monitoring.

Brain protection: what are going to do?

A. Propofol? No effect of intraoperative brain protection with propofol on postoperative cognition in patients undergoing temporary clipping during intracranial aneurysm surgery or following valve surgery
B. Desflurane? Maybe, but impairs ability to monitor MEPs
C. Hypothermia? No!
D. Hypertension? Good to try when monitoring suggests ischemia
E. Ketamine? 0.5 mg/kg IBW; Hudetz et al, at least for CP bypass
F. Clot retrieval: I like MAC, but no prospective data to support

Reduced risk of post-operative delirium

• BIS 40-60 during surgery
• MABP 80; certainly greater than 55 mmHg
• Consider IV Lidocaine infusion
• Consider IV Ketamine 0.5 mg/kg (Single dose)??
• Consider IV dexmeditomidine infusion (1 mcg/kg over 10 min at the end of the case, post-operative or intra-nasal)
Thank you!
kirschje@ohsu.edu