Anesthesia and NIOM

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Objectives/Outline

- Modalities monitored
- Anesthetics influence
- Cases Examples

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NIOM

- Continuous assessment of the nervous tissue functional integrity (monitoring)

Identification of functionally normal or abnormal nervous tissue (mapping)

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Types of Positive Mapping

- Motor cortex:
  - direct cortical
  - direct subcortical
- Language
- Identification of seizure foci
- Central Sulcus Localization (phase reversal SEP)
- Brainstem (Direct Brainstem Stimulation)

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IOM modalities

- SEP : *transcranial and direct cortical*
- MEP : *transcranial and direct cortical*
- EMG :
  - *Free Run*
  - *Triggered*
- BAEPs
- Functional Cortical Mapping
- EEG
- NAP

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Most Frequently Used Anesthetic Groups in NIOM:

- TIVA (total intravenous anesthesia)
- Inhalational agents
- Muscle relaxants
- Other

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What Kind of Changes are Expected with Anesthetic Effect?

Diffuse or Focal

Symmetric or Asymmetric

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Anesthetic Principles Considerations

- More synapses, longer pathways=more effect of anesthetics
- Greater lipid solubility of anesthetic=greater effect

"Consciousness and Anesthesia"

Alkire et al. Science, 2008

Table 1. Ionic mechanisms and targets of current clinical anesthetics

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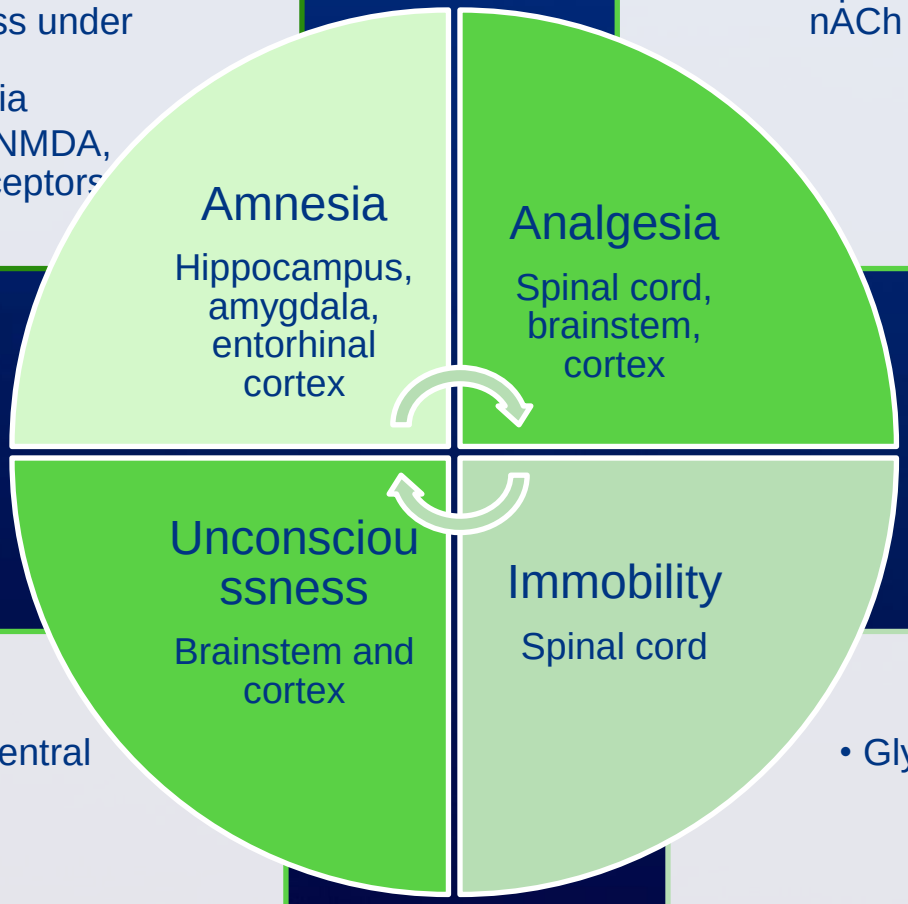
Anesthesia Goals

- Accidental awareness under general anesthesia
- GABAa, NMDA, nACh receptors

- Opioid, NMDA, nACh



- GABAa, central a2

- Glycine>GABAa

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Anesthetic Principles Considerations for SEPs

- Cortical responses affected most/first
- Most anesthetics produce dose dependent decrease in amplitude and increase in latency
- Exceptions: etomidate and ketamine
- Effects are variable among patients

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Ketamine an etomidate

Etomidate

- GABA inhibition but at low doses excitatory cortical effect
- Increases SEP amplitudes
- Epileptogenic at low doses
- Decreases ICP without drop in MAP
- Concern for adrenal suppression

Ketamine

- NMDA inhibition at low doses
- Increases SEP amplitudes
- Decreases seizure threshold in patients with epilepsy
- Can increase ICP
- Causes hallucinations

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SEPs Anesthetic Effect

	Cortical	Subcortical	Peripheral
Halogenated gases	decr. amp, inc. lat	min change	no change
Nitrous oxide	decr. amp, -lat	min change	no change
Propofol	min change	min change	no change
Opioids	min change	min change	no change
Benzodiazepines	min change	min change	no change
Muscle relaxants	inc. amp, -lat	inc. amp, -lat	no change

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Inhalational Agents Effect on SEPs Cortical Potentials

”Anesthesia for Intraoperative Neurophysiologic Monitoring of the Spinal Cord”

Sloan TB et al., J Clin Neurophysiol. 2002

Fig. 1 and 2

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”Nitrous Oxide and Isoflurane are Synergistic with Respect to Amplitude and Latency Effects on Sensory Evoked Potentials”

Sloan et. al, J. Clinical Monitoring and Computing, 2010
Fig. 3

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MAC (Minimum Alveolar Concentration)

- MAC is the alveolar concentration that prevents movement in response to surgical incision in 50% of patients anesthetized with *gas alone*

- MAC examples:
  - Isoflurane 1.2%
  - Sevoflurane 2.0%
  - Desflurane 6.0%

- A lower MAC means a more potent agent, not a better agent

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Factors That Alter MAC Norms

INCREASE

- Infant (peak 6 mo.)
- Chronic ETOH
- Hypernatremia
- Hyperthermia

DECREASE

- Acute ETOH
- Elderly
- Hyponatremia
- Hypothermia
- Anemia
- Hypercarbia
- Pregnancy

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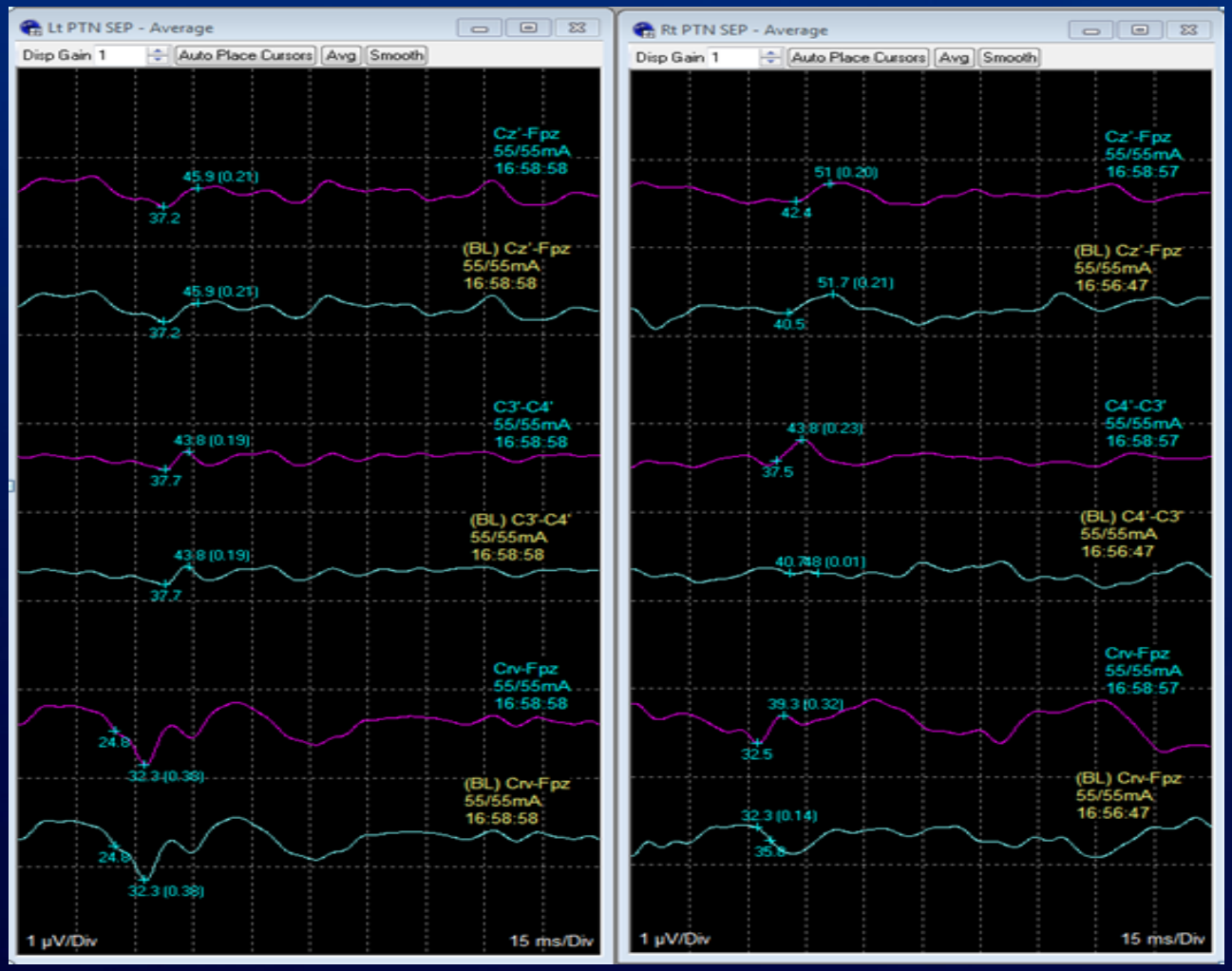
Case Example 1

What if you start a case with these baselines? Can you be reliable for positioning?



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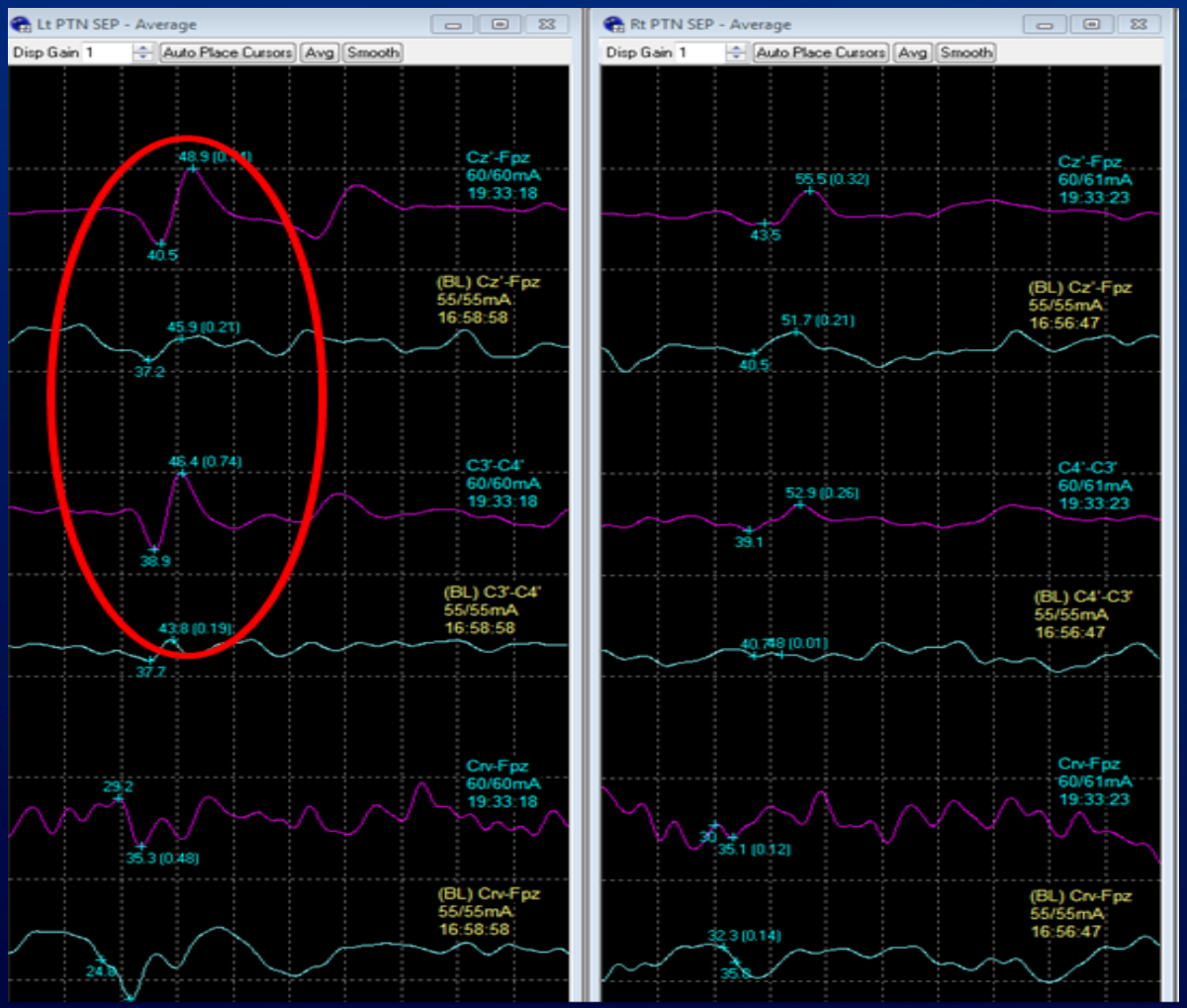
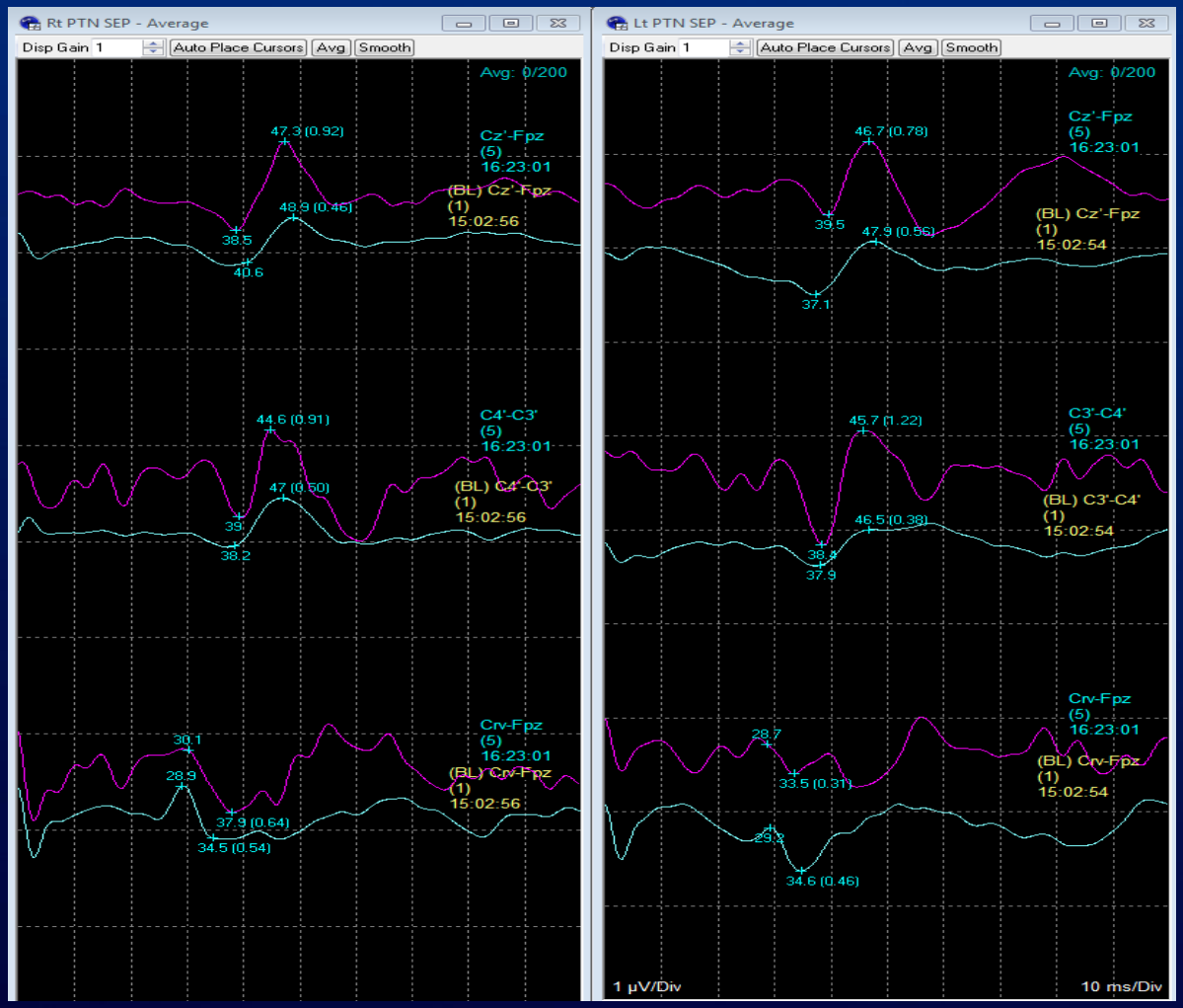
And 1 hour later SEPs improved during opening

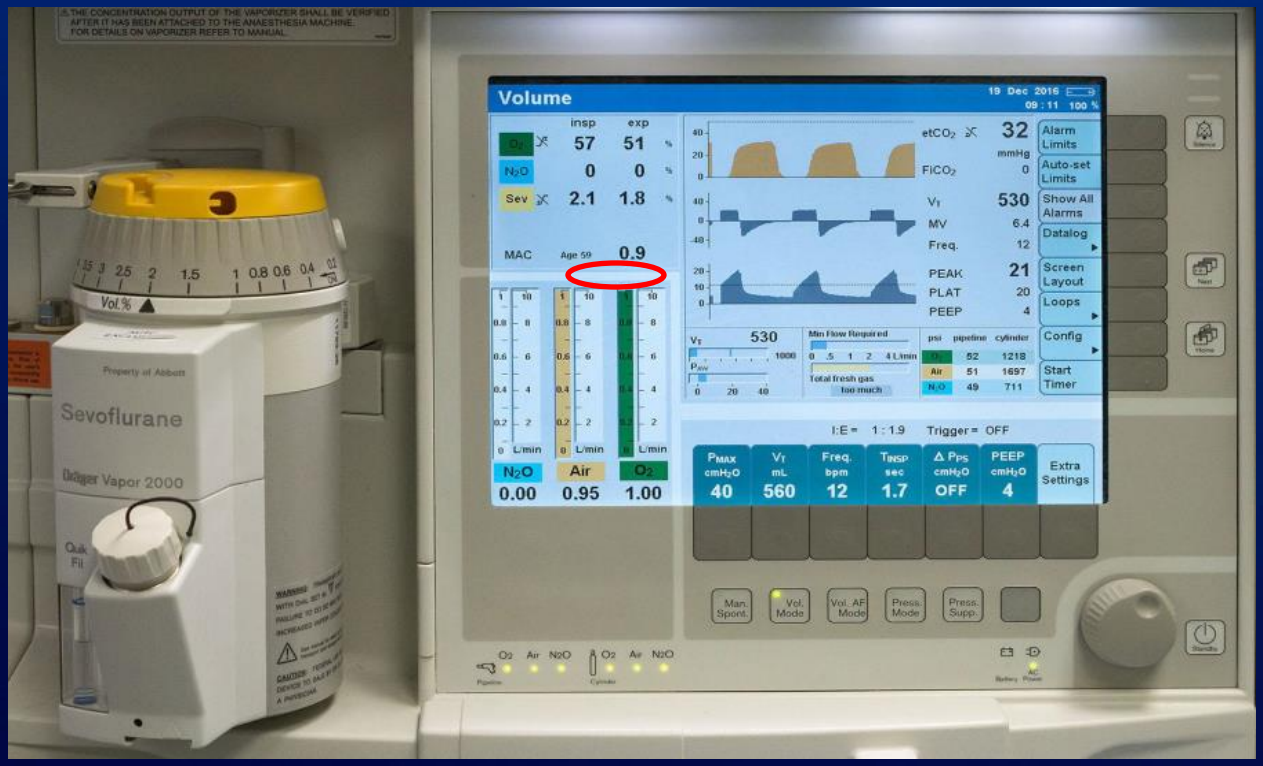


Case Example 2

SEPs improved (from baselines) during opening?



What is your next step after you have completed extensive troubleshooting and everyone is looking in your direction waiting to report baselines and position the patient?



Propofol

- Sedative and amnestic, minor analgesic and immobility effect
- GABAa agonist
- Decreases CBF and ICP and may be protective in focal ischemia
- Decreases systemic blood pressure by arterial and venodilation
- Advantage of short half life, rapid on and off set and antiemetic properties

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Propofol cont.

- Plasma concentrations rise at constant infusion rates
- Minimal effect on cortical SEPs
- Attenuates MEPs but when used with opioids, permits monitoring
- Depressant effect may be synergistic with other agents
- Rapidly metabolized, but also redistributes to fatty tissue – including brain
- Propofol infusion syndrome

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Remifentanyl

- Half-time is nearly constant at 4 min
- Can be used at relatively high doses, lowering dose of hypnotic or gas
- Needs no dose adjustment for liver or renal disease

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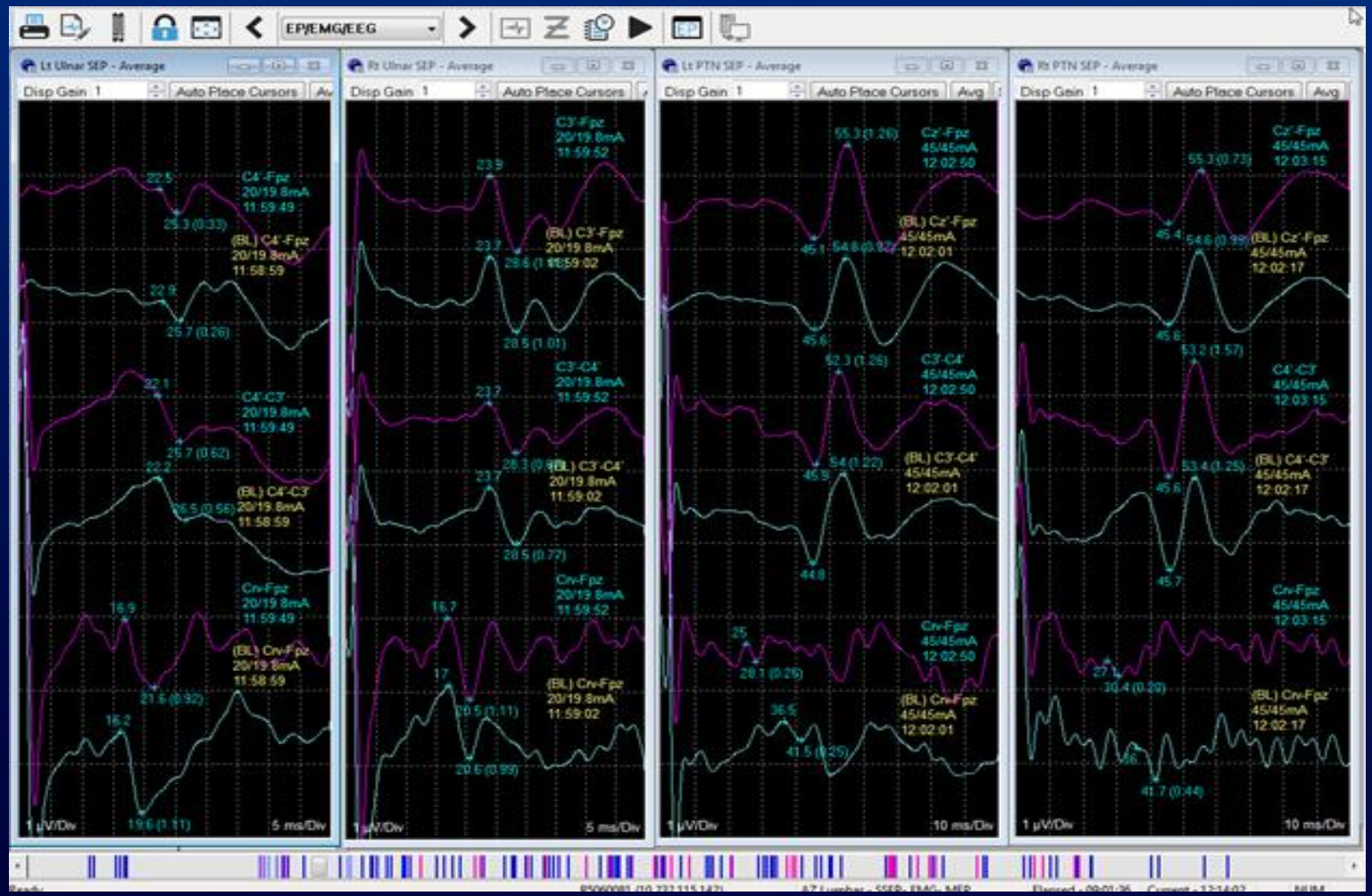
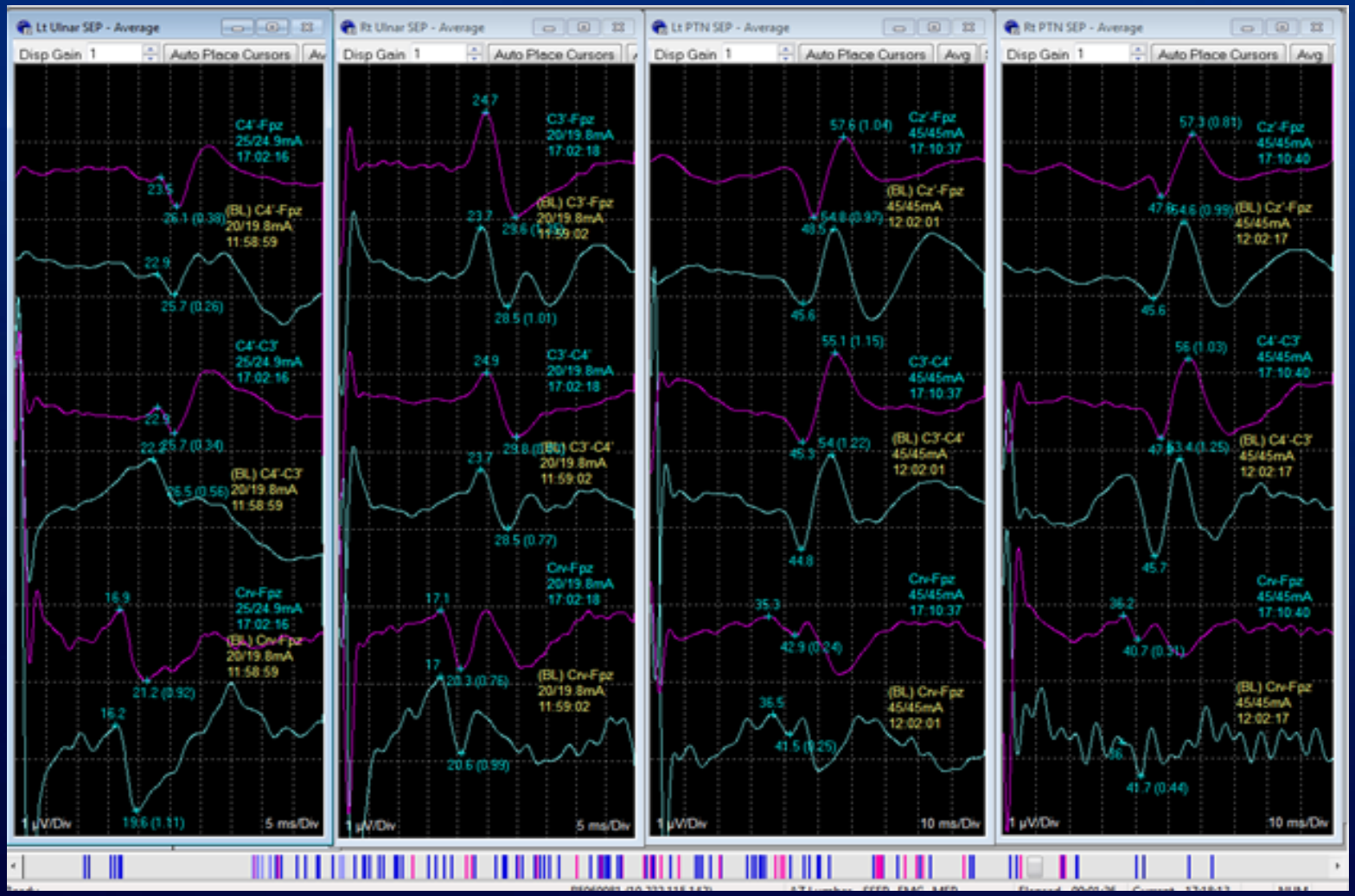
Case Example 3

SEP Baseline with TIVA



Closing SEPs, data stable after few hours of TIVA



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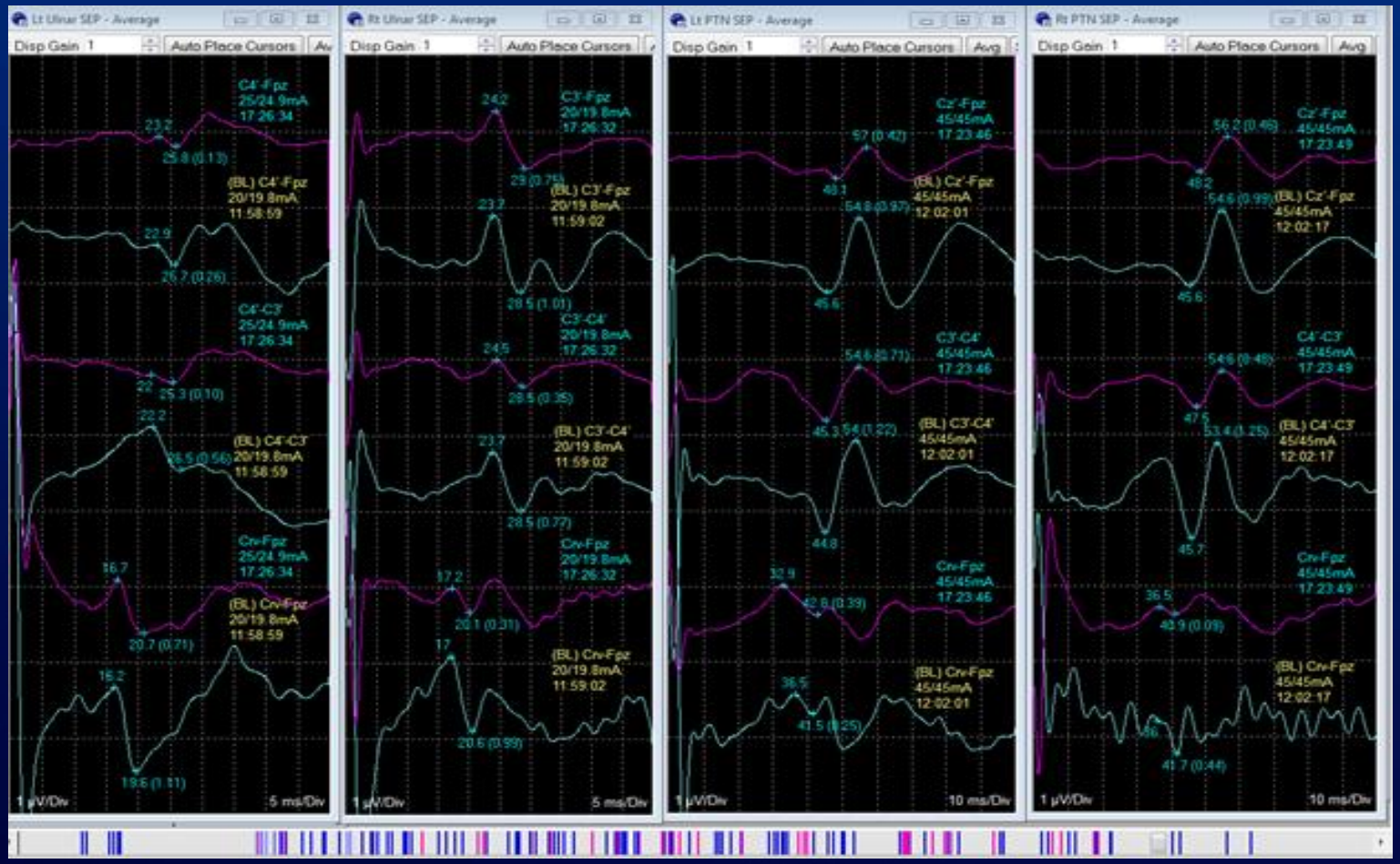
SEPs 8 min after TIVA off and Gas on (sevo 0.5 MAC and N2O 50%) for closing



MEPs

- Electrical pulses delivered to motor cortex
- Signal is generated in the motor cortex and recorded from spinal cord

Directly:

- D-wave

Indirectly:

- Peripheral nerve -->muscle (CMAP)

Deletis, Sala at al. 2009

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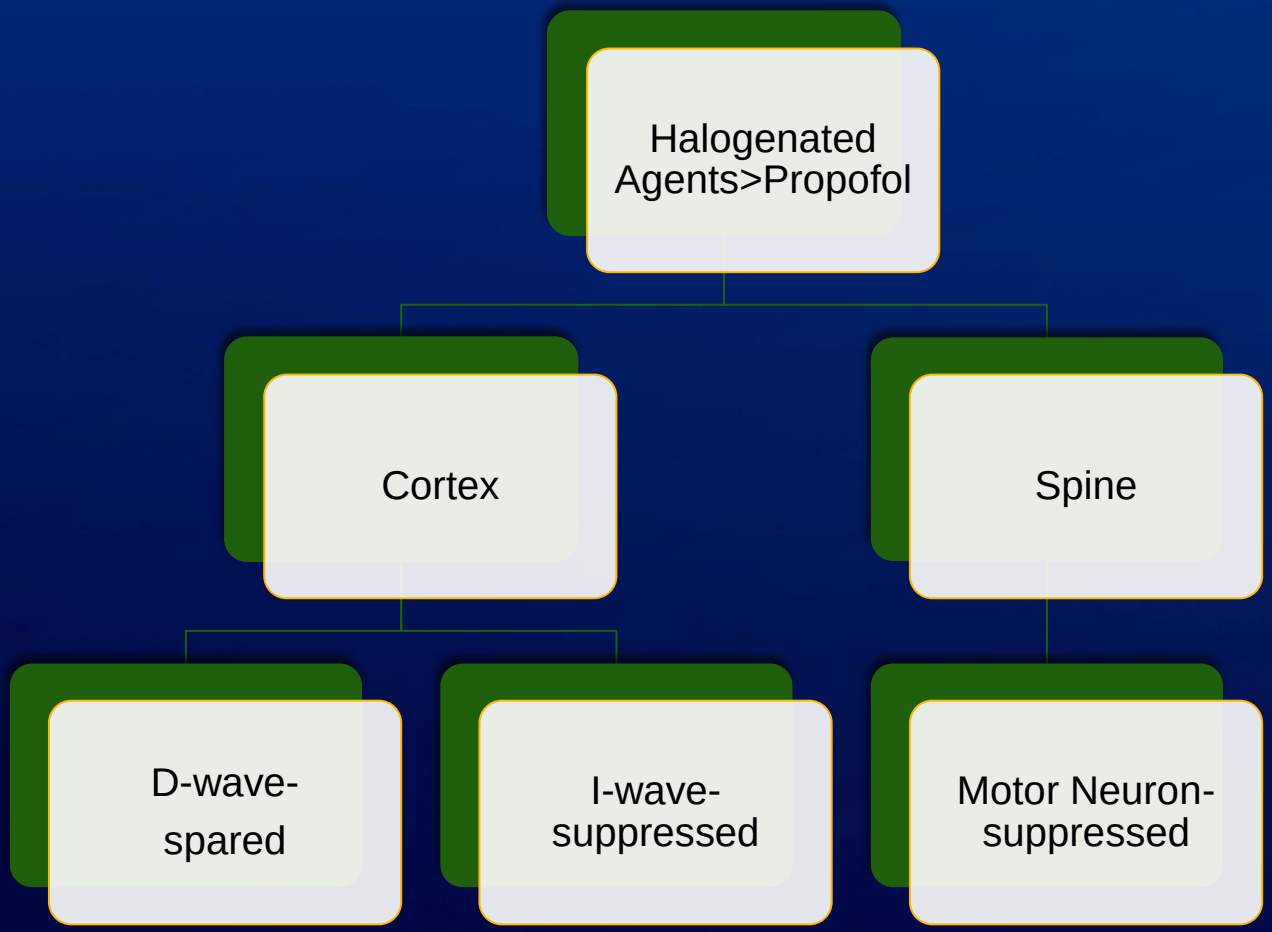
Main Sites of MEP Attenuation with Anesthetics



Degree of Muscle MEP Suppression

- Potent halogenated agents, nitrous oxide
- Moderate propofol, benzodiazepines
- Little etomidate, ketamine, narcotics

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MEPs
and

Ethomidate

- Dose-dependent increase, then decrease of MEP amplitude
- Low dose increases I waves
- High dose decreases I waves

Ketamine

- Dose-dependent suppression of MEPs

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Effect of Inhalational Agents on MEPs

- Monitoring: increased baseline threshold stimulation intensity for TcMEPs
- Mapping : increase in threshold for direct cortical motor responses and increase risk of triggering seizures
- Risk for false negatives with negative mapping due to increase motor mapping threshold (plus dexmedetomidine)

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”Anesthesia for Intraoperative Neurophysiologic Monitoring of the Spinal Cord”

Sloan TB et al., Journal of Clinical Neurophysiology

Fig. 4 and 5

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MEPs and Propofol

- Boluses around positioning can cause tricky changes
- Boluses around critical parts can cause changes
- In overweight patients decrease in propofol infusion rate will not necessarily result in MEP improvement-because of redistribution
- Estimated threshold for MEP stimulation will be higher with burst suppression

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Anesthetic Fade

- MEP responses have been observed to deteriorate over the duration of surgery under general anesthesia
- McDonald et al. described “fading MEP” with prolonged exposure to anesthesia
- Lyon et al. reported that muscle MEPs tend to exhibit gradually rising thresholds throughout surgery despite stable anesthesia
- Threshold increases with duration of anesthesia independently of dose-dependent depressant effects
- Lipid soluble and insoluble agents

Lyon R. J Neurosurg Anesthiol 2005;17:13-19

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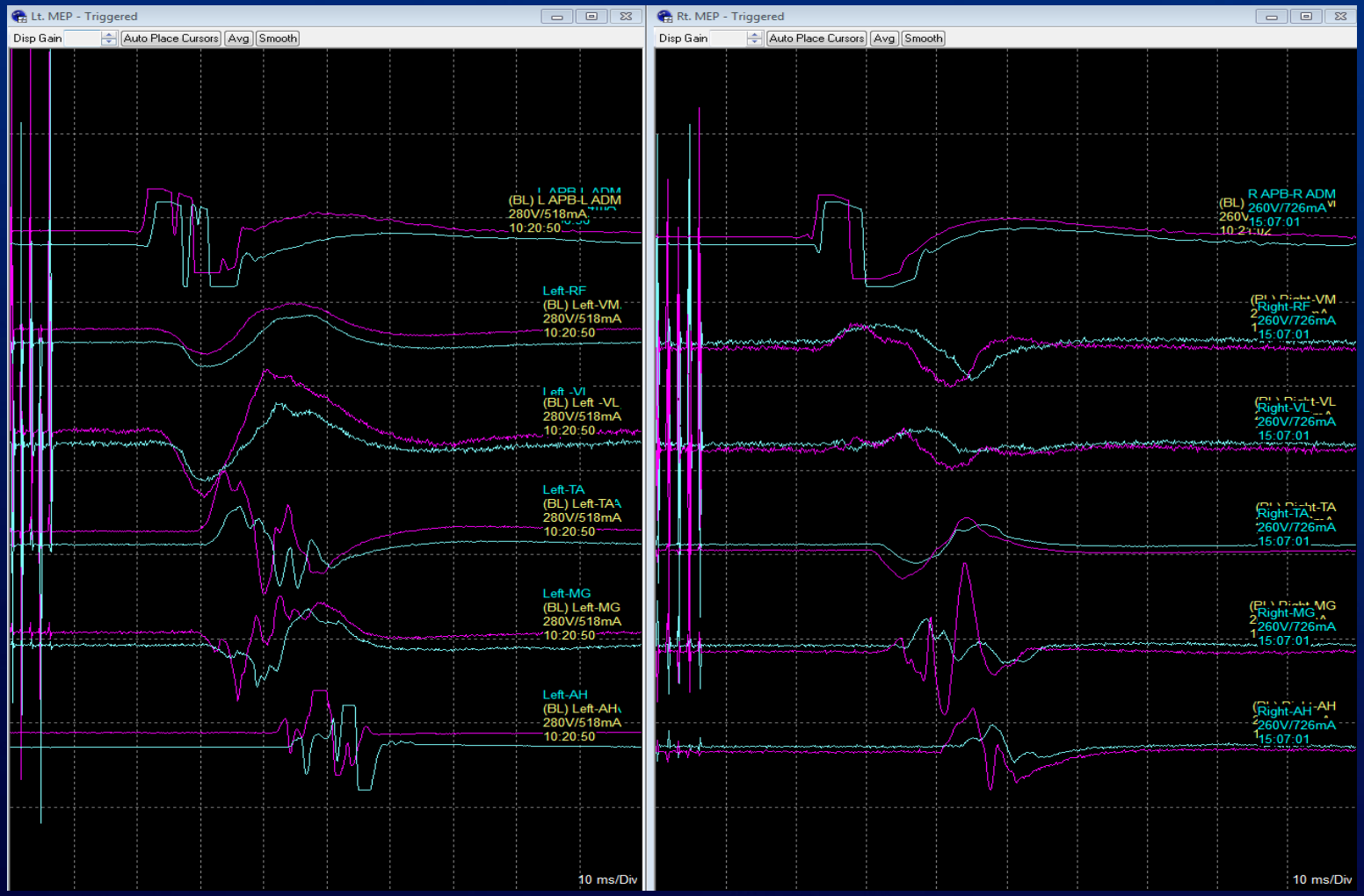
Case Example 4

MEPs stable with 6 hours of TIVA



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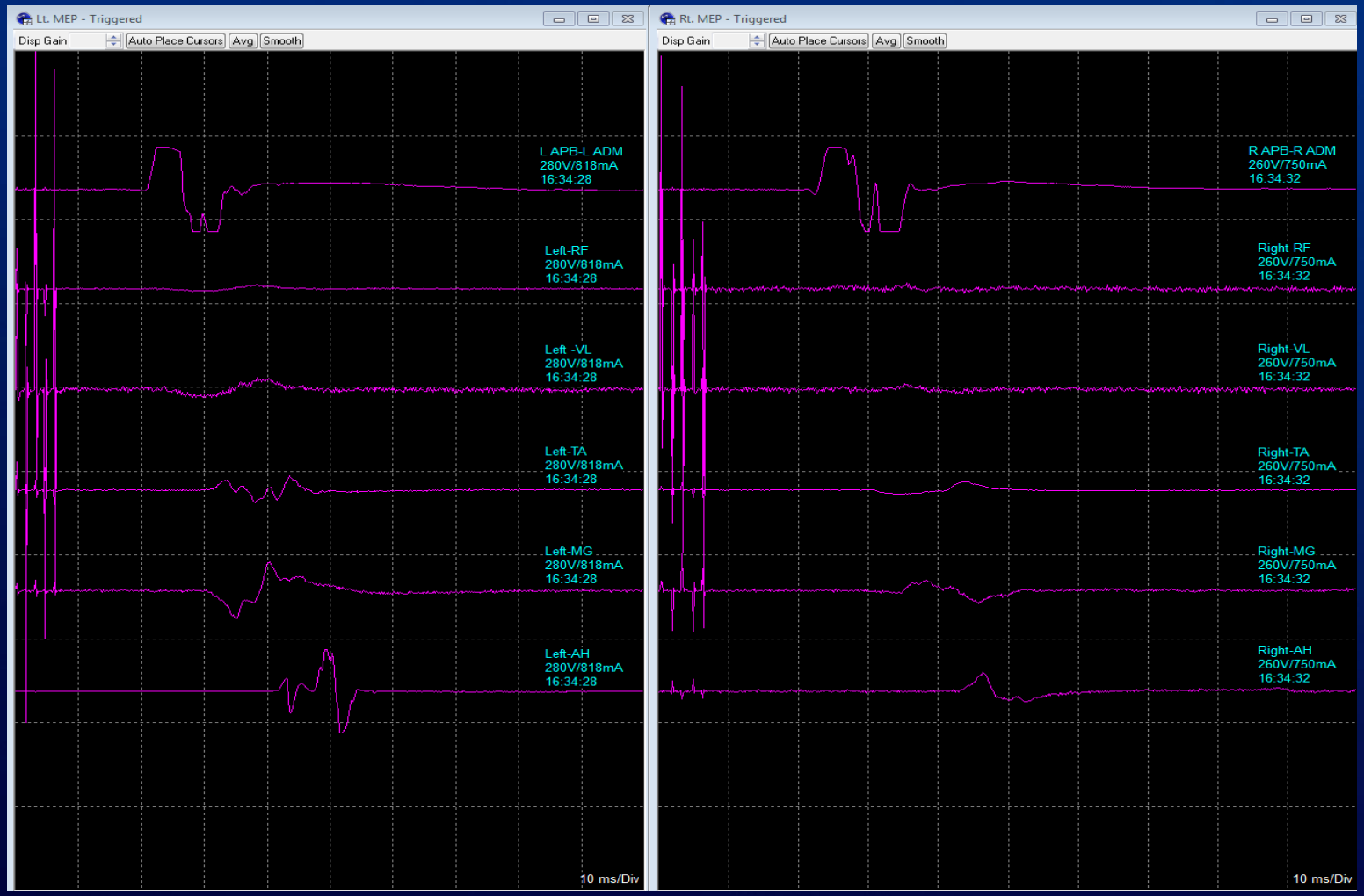
TIVA off for 1 hour due to switching to 0.5 MAC sevoflurane



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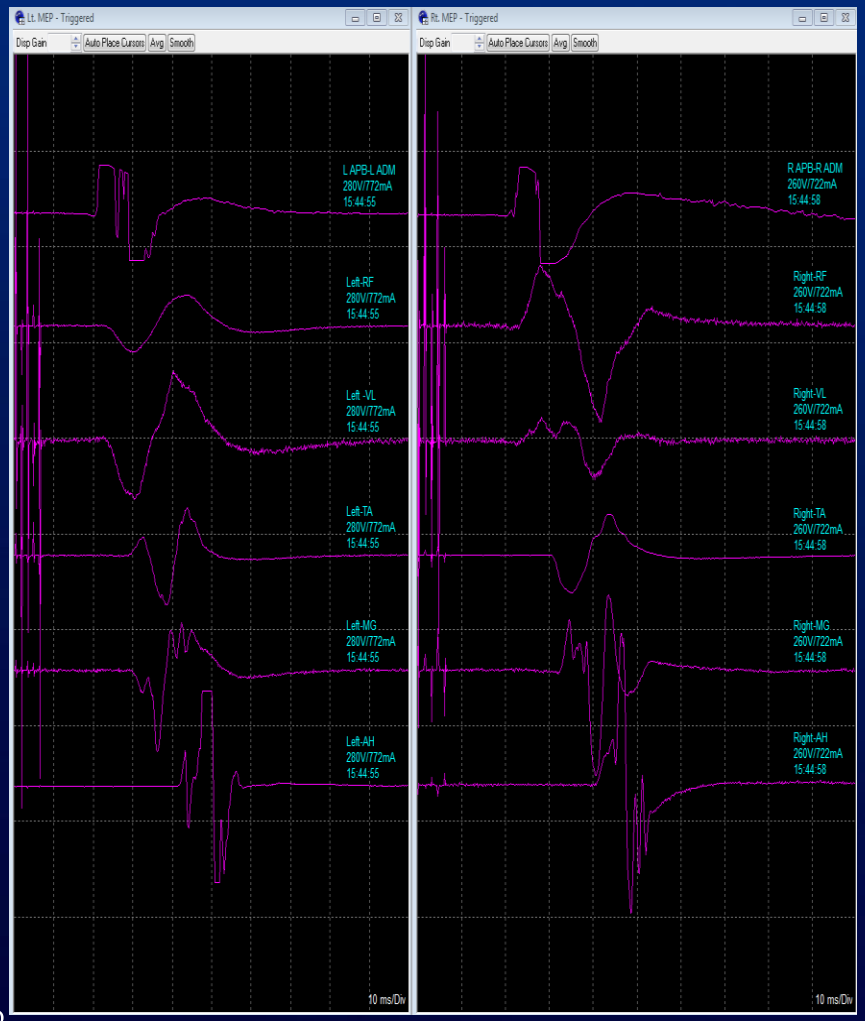
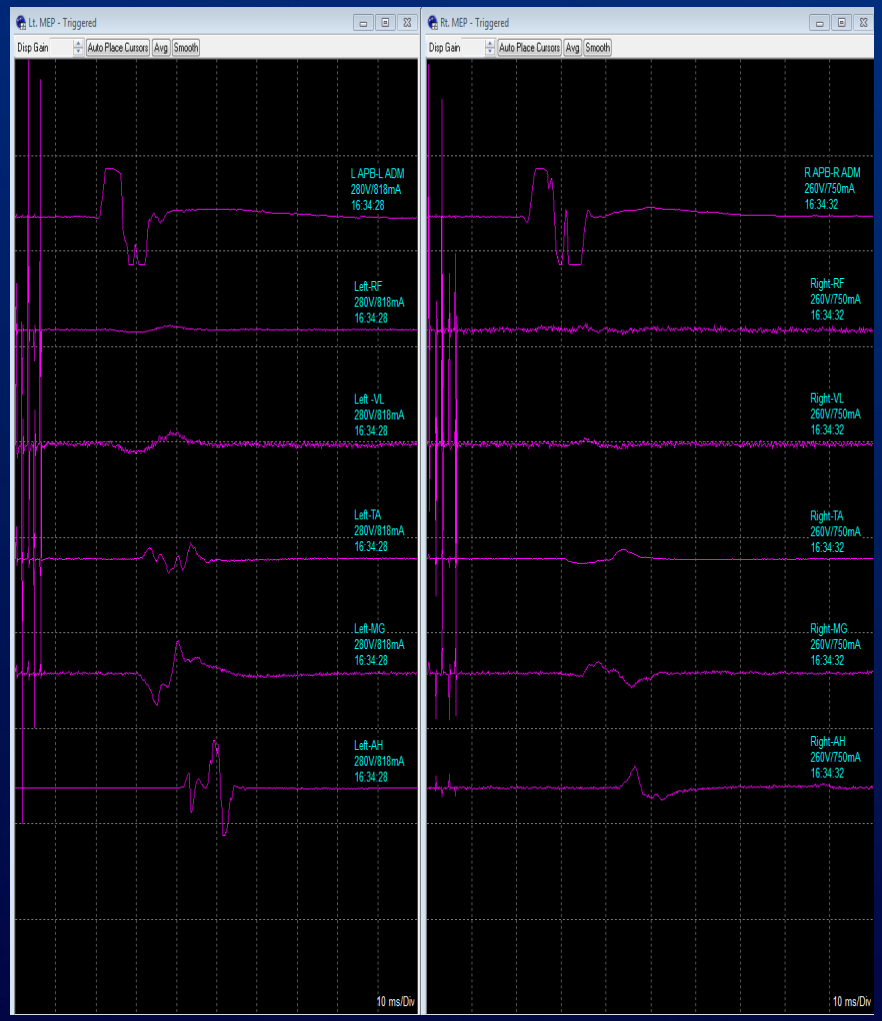
Pre and post switching to sevoflurane





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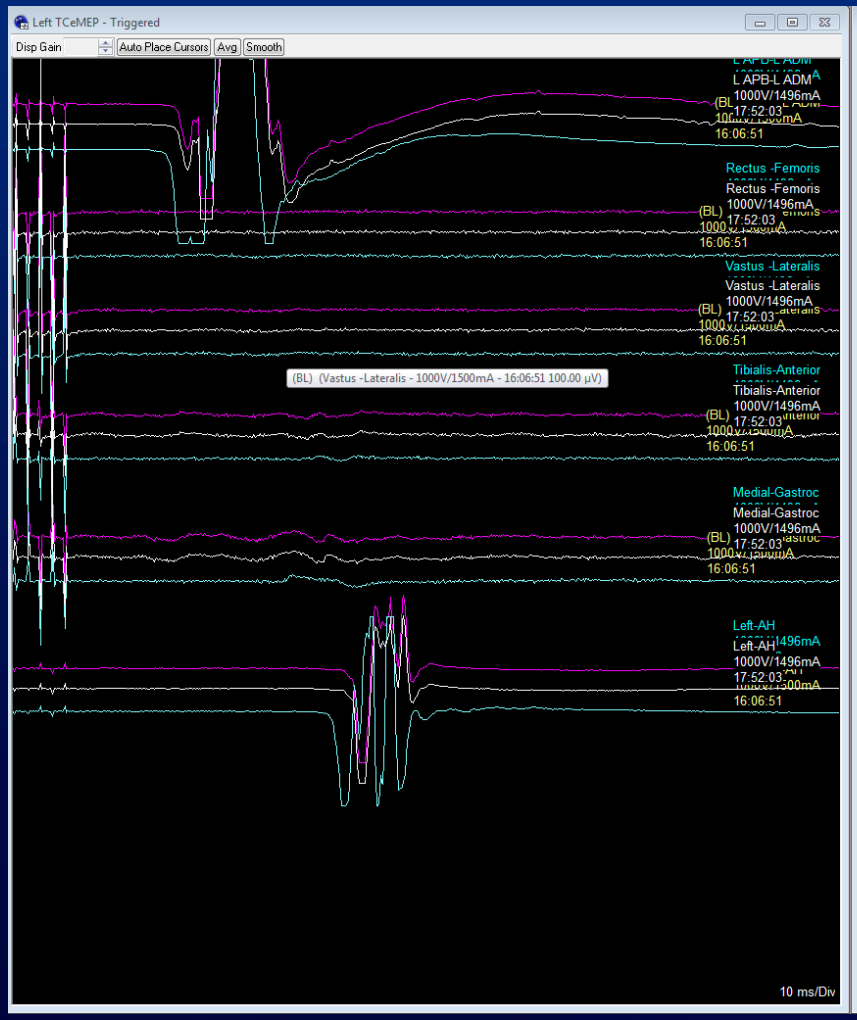
Case example 5

MEPs baselines



mins

07:15

35 mg
ng
g
mcg
268 mcg
416 mg
ng
ng
L
mL

1 mg
1 mg
100 mcg
0.6 mg
58.8 mcg
5.88 mcg/Min
352.8 mg/Hour
140 mg
40 mg
50 mg
0 mL/Hour

			36.43	36.37	36.17	36.13	36
		1.4	2.9	3	3.1	2.3	1.3
		0	3.5	3.5	3.6	2.2	1.1
			SR			SR	
0	0	2.5	1.2	1.2	1.2	1.2	1.1
0	0	0	0	0	0	0	0
	68	66	81	78	74	75	60
0.06	9.4	1.5	0.75	0.75	0.75	0.75	0.7
	99	98	51	48	47	47	50
		604	388	383	382	442	422
		24	13	13	12	15	14
		5	4	4	4	4	4
		5	12	12	10	10	14

Baselines and Critical Part of Surgery

- A structure with “limited reserve” at baseline is more and faster affected by anesthetic effect
- Recovery of signals from the effect of anesthetic may require time (30 min or more) which can fall on the critical part of the surgery
- During this time it would not be possible to detect whether there is a concomitant surgical injury

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Previous Studies and Quantified Effects of Anesthesia during IOM

- Pechstein et al 2014 : distinct motor responses were recorded in:
  - 88% (15 of 17) of patients with TIVA
  - 8% (1 of 13) of patients with nitrous oxide and halogenated inhalational agents
- The range of MEP amplitudes with the administration of an inhalational agent may indicate enhanced spontaneous fluctuation of motor neuron excitability (Pelosi et al., 2001)

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“Differential rates of false-positive findings in transcranial electric motor evoked potential monitoring when using inhalational anesthesia versus TIVA during spine surgeries”

Tamkus AA et al, Spine J. 2014

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Tamkus AA et al, Spine J. 2014

- Patients with inhaled anesthesia showed significantly higher rates of false-positive TcMEP changes (15.0% vs. 3.2%) compared with the TIVA group
- These differences were significant across all surgical subgroups
- The inhaled group had a larger number of patients with preoperative motor deficits compared with TIVA (45.0% vs. 37.4%), a potential confounder for false-positive results
- Significantly higher rate of false + TcMEP changes was still observed in the inhaled group (11.4% vs. 0.6% for TIVA) when analyzing only those patients without preoperative motor deficits

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Tamkus AA et al, Spine J. 2014

CONCLUSIONS: Use of inhalation anesthesia during adult spinal surgery is associated with significantly higher rates of false-positive changes compared with TIVA during Tc-MEP monitoring. This relationship appears independent of preoperative motor status. The potential confounding effects of inhalational anesthesia on TcMEP monitoring should be considered when determining anesthetic regimen

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”Transcranial motor evoked potentials during anesthesia with desflurane versus propofol – A prospective randomized trial”

Malcharek et al. 2015, Journal of Clinical Neurophysiology

- MEPs recorded using combination of remifentanil/desflurane or remifentanil/propofol by analyzing peak-to-peak amplitudes
- Baseline small MEP amplitudes suggested monitoring with propofol/remifentanil-TIVA rather than desflurane anesthesia
- To ensure intraoperative sensitivity to MEP changes and clear interpretation of surgical events study design in patients undergoing carotid surgery without preoperative motor deficits

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“Exemplarily Development of tcMEP Amplitudes from Abductor Digiti Minimi Muscle Under (a) Desflurane/Remifentanil and (b) Propofol/Remifentanil Anesthesia”

Malcharek et al. Clinical Neurophysiology, 2015
Fig. 2

Remifentanil 0.5 µg/kg/min
Desflurane 4 Vol%/ 0.5MAC
MAP 78 mmHg
FiO2 50 %
etCO2 31 mmHg
Temperature 35.5° C

Remifentanil 0.5 µg/kg/min
Propofol 5 mg/kg/h
MAP 82 mmHg
FiO2 50 %
etCO2 31 mmHg
Temperature 35.6° C

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”High-frequency Stimulation Restored Motor-evoked Potentials to the Baseline Level in the Upper Extremities but not in the Lower Extremities under Sevoflurane Anesthesia in Spine Surgery”

Shida et al. J Neurosurg Anesthesiol. 2012

- Shida et al. (2012) published data concerning the differences in MEP amplitudes depending on both sevoflurane/remifentanil and propofol/remifentanil protocols with similar results and found significantly higher amplitudes during propofol/remifentanil anesthesia recording tcMEPs from both upper and lower extremities

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Dexmedetomidine

- Analgesic, sedative
- Selective alfa2 adrenergic agonist
- Anti-inflammatory
- Useful in opioid resistant patients
- Side effects: hypotension, bradycardia
- Affect MEPs, especially after long duration infusion at high doses
- Has a long half life and thus stopping will not result in prompt improvement of MEPs
- Decreasing propofol instead can be tricky as patient may wake up (dexmedetomidine is an anlgesic/sedative but not a potent anesthetic as propofol)

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Dexmedetomidine-related Loss of MEPs

Case Report
13 y/o 90 kg
MEP loss at higher Dex. dose with other drugs
SEP shows no change
Propofol 100 µg/kg/min
Remifentanil 0.5 µg/kg/min
Dexmeditomidine 0.5 µg/kg/hr

”Loss of Transcranial Electric Motor Evoked Potentials during Pediatric Spine Surgery with Dexmedetomidine”

Mahmoud et al. Anesthesiology 2007

Fig. 1.

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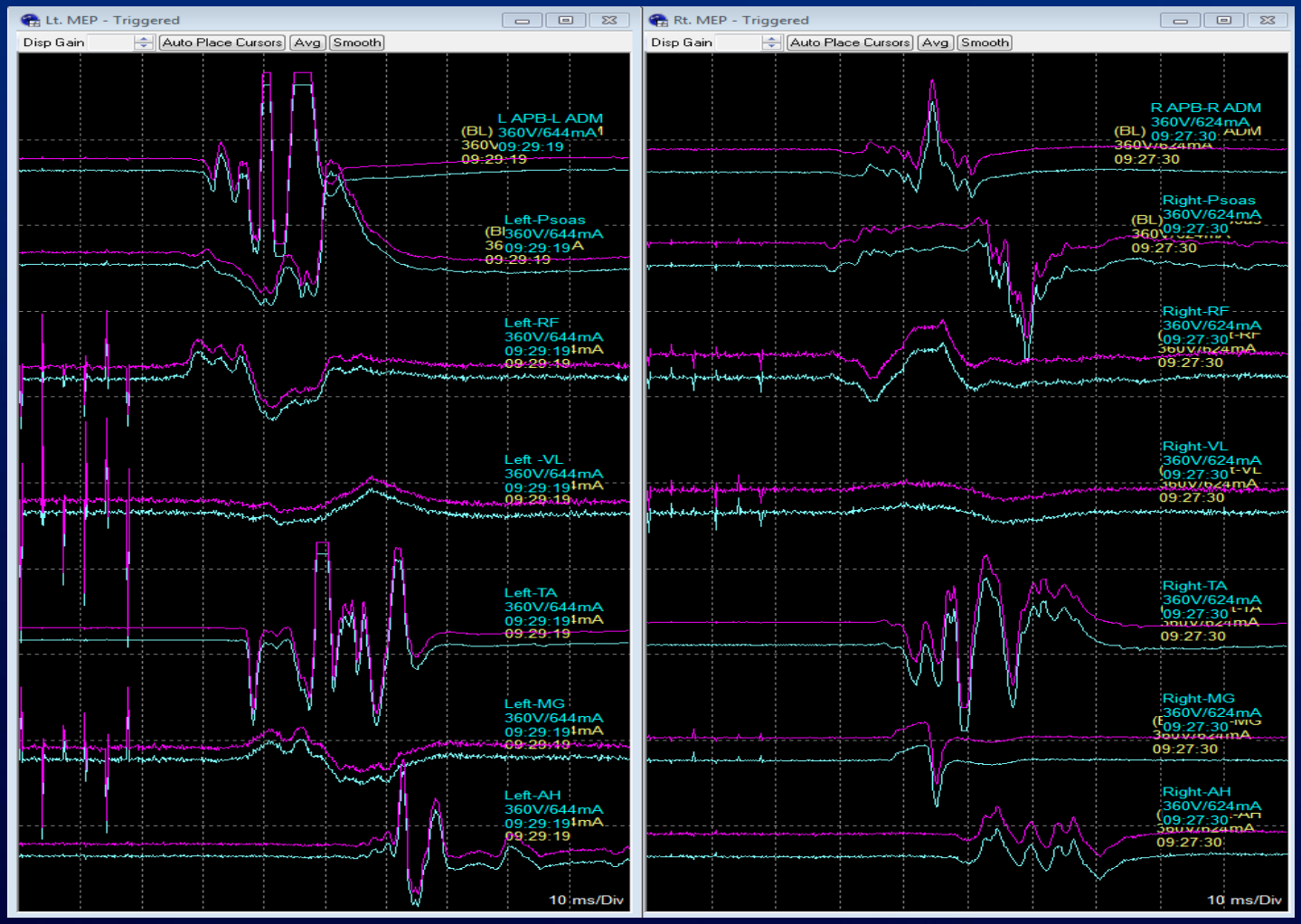
Case Example 5

PSF T4-ilium

Baseline MEPs with dexmedetomidine at 0.4 mg/kg/hr, stim. 360 V bilaterally



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Change in MEPs with increased stim by 200V on the right 30 min later

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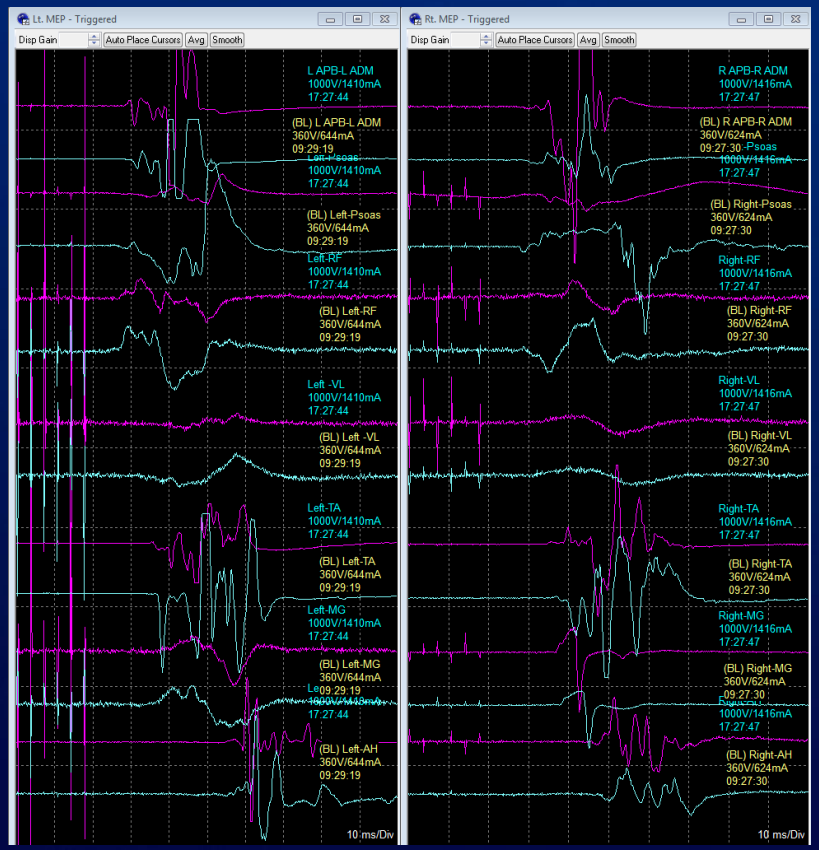
Max stimulation on the right

Recovery after dex. stopped



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What are the NIOM signs of patient being light?

- EEG
- Free run EMG muscle activity
- Increased artifact on the SEP recordings

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Sequence of Changes during EEG with Progression of Anesthesia

- Mild slowing with superimposed fast activity
- Increase in slow frequencies
- High amplitude diffuse delta slowing
- Burst suppression

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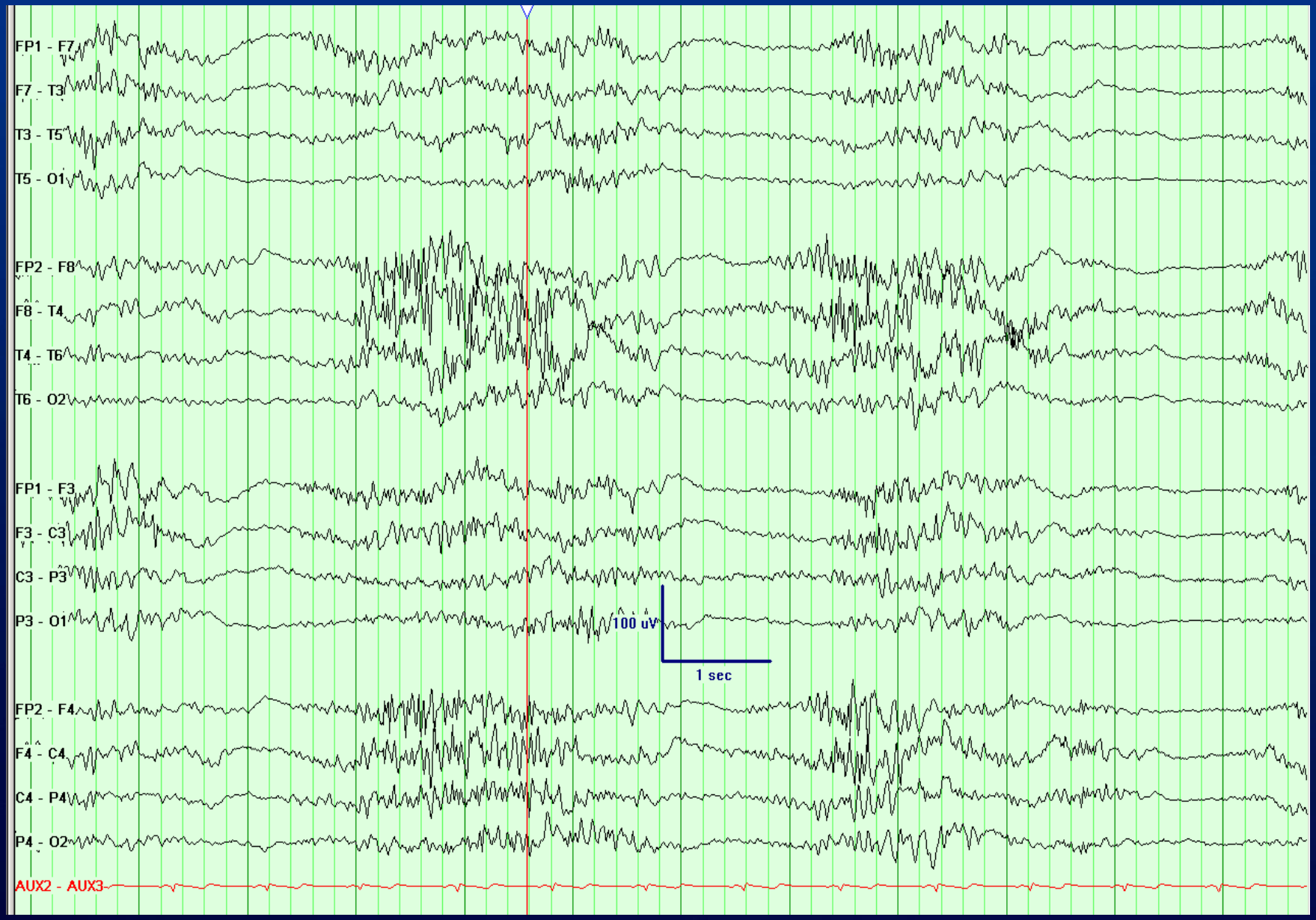

Simon MV, 2010

EEG Suppression

- Estimated threshold for MEP stimulation will be higher with burst suppression
- Ketamine alters EEG to show more fast frequencies (beta) and less suppression
- Propofol and ketamine infusion may make EEG look “lighter”-less burst suppression and thus can be misleading (while the spinal cord alpha motor neuron excitability can be suppressed)

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EEG and

- Opioids:
  - Dose related decrease in frequency ->delta
  - Do not produce burst suppression
  - Since don’t suppress EEG, are often used during ECoG

- Dexmedetomidine:
  - Spindle-like activity on slow waves ~ Stage 2 sleep at low doses
  - Resembles slow wave sleep at higher doses
  - Does not produce burst suppression used alone

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What Regimen is Better for EEG Monitoring?

1. Inhalational agents
2. TIVA (propofol and opioid)

- What if you have to monitor both SEP and EEG?
  - Titrate to strike a balance

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BAEPs, Anesthetic Applications

	Generator
I	Distal CN VIII and nucleus
II	Distal CN VIII
III	Lower pons
IV	Rostral pons or mesencephalon
V	Mesencephalon

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BAEP

- Highly resistant to anesthesia
- Each patient is his/her own control
- Follow both latencies and amplitudes

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Quiz:
Which Factor Affects BAEPs Most?

1. High dose inhalational anesthetic
2. High dose propofol
3. Hypothermia
4. Muscle relaxant

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Anesthetic Consideration in Brainstem Monitoring

- Any type of anesthesia aside for neuromuscular blockade is compatible[1]

- Motor cranial nerve EMG activity can usually still be monitored in the presence of NMB agents, since NMB agents have more effect on limb rather than cranial muscles[2]…not recommended

1. Morota, 2002; 2. Harper, 1998

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Muscle Relaxants

- Free run EMG
- Triggered EMG
- MEPs

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Neuromuscular Blocking Agents

Depolarizing

Depolarize cell membrane of the skeletal muscle fiber

- Succinylcholine

Non-depolarizing

Reversibly bind to post-synaptic ACh receptors

- Rocuronium
- Vecuronium
- Atracurium
- Pancuronium
- d-tubocurarine

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Neuromuscular Blocking Agents

”Pharmacology of Neuromuscular Blocking Drugs”

Continuing Education in Anaesthesia Critical Care & Pain, 2004

Table 1

Neuromuscular Blockade

SEPs

- Improves SEP recordings (especially subcorticals) by reducing muscle artifact

MEPs

- Attenuates
- For spinal cord monitoring <75% blockade
- May increase variability

Free run EMG

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Nondepolarizing NMBA Reversal

- Neostigmine
  - Acetylcholinesterase inhibitor
- Onset ~ 1 min
- Peak effect ~ 9 min
- Duration ~ 20 – 30 min
- Usually incomplete/ineffective with deep blockade (0 twitches on TOF)
- Muscarinic side effects(bradycardia, bronchconstruction, QT, salivation, nausea, vomiting.....)

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Sugammadex-nondepolarizing NMBA Reversal

- Cyclodextrin antagonizes steroidal NMBD by encapsulating and inactivating them
- No effect on AChE, so no muscarinic side effects
- FDA approved 2015
- Reliably and completely reverses profound neuromuscular block without cardiovascular or other effects
- Ineffective against atracurium (isoquinoline derivative) so can be used for reblockade!
- No effect on succinylcholine

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Case Example 6

73 y/o F with balance/coordination disturbances and frequent recurrent falls

No weakness

No sensory deficits at baseline

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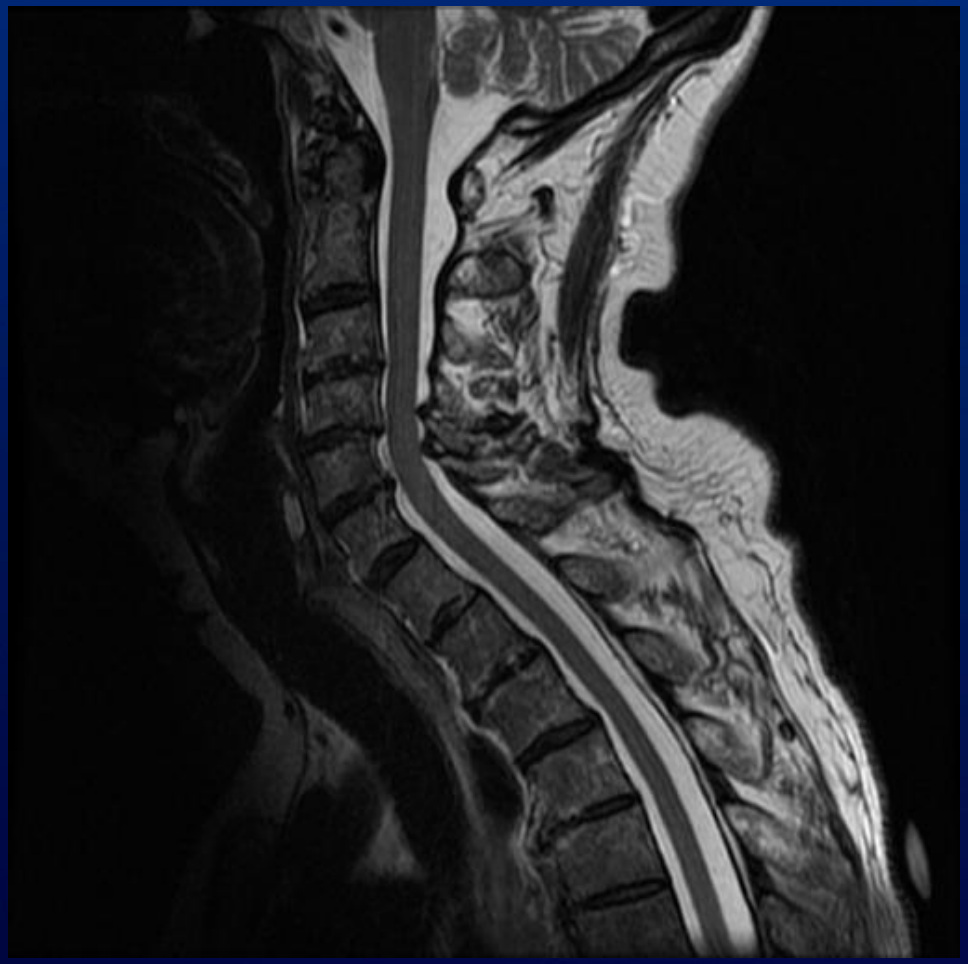
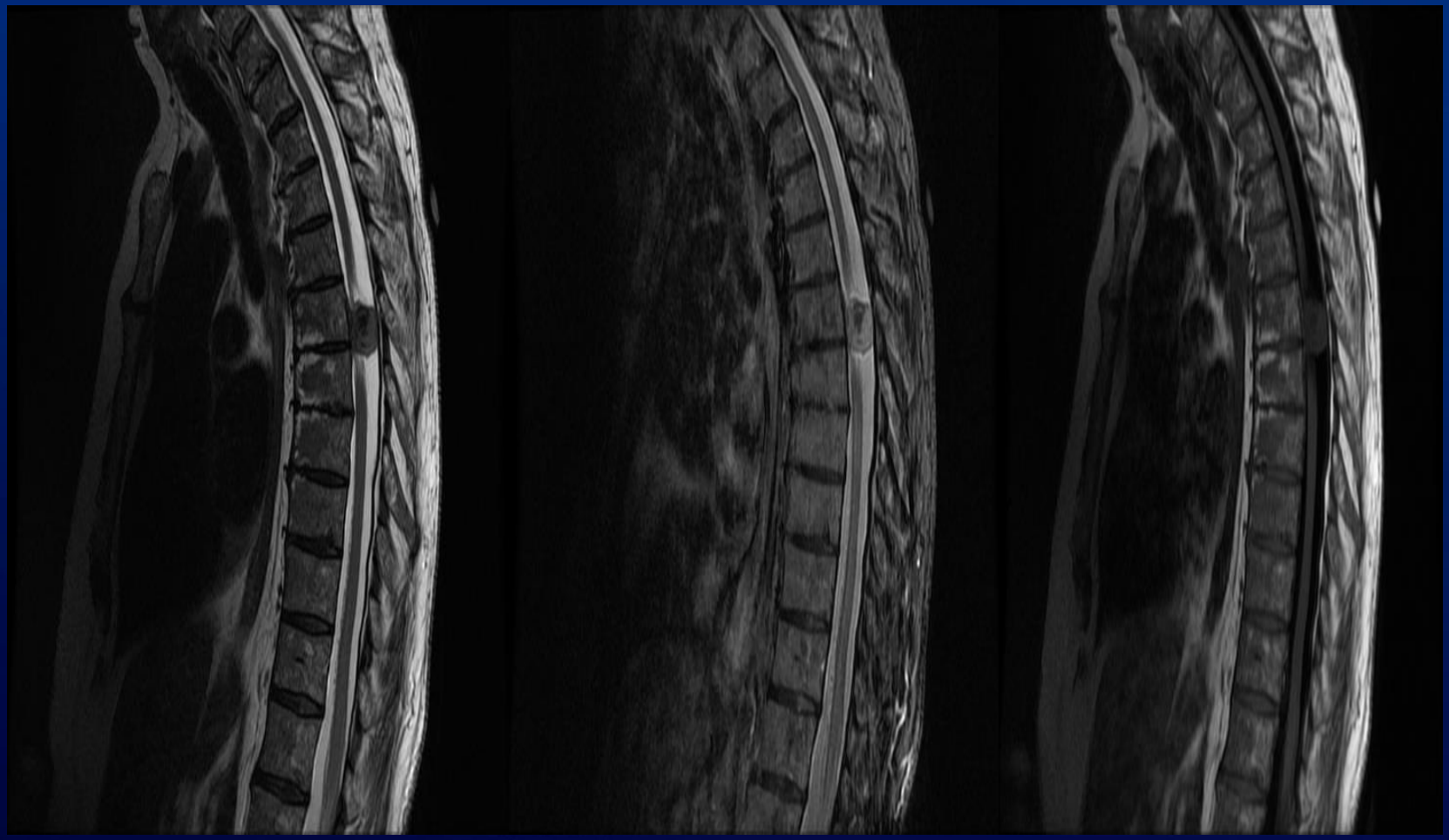
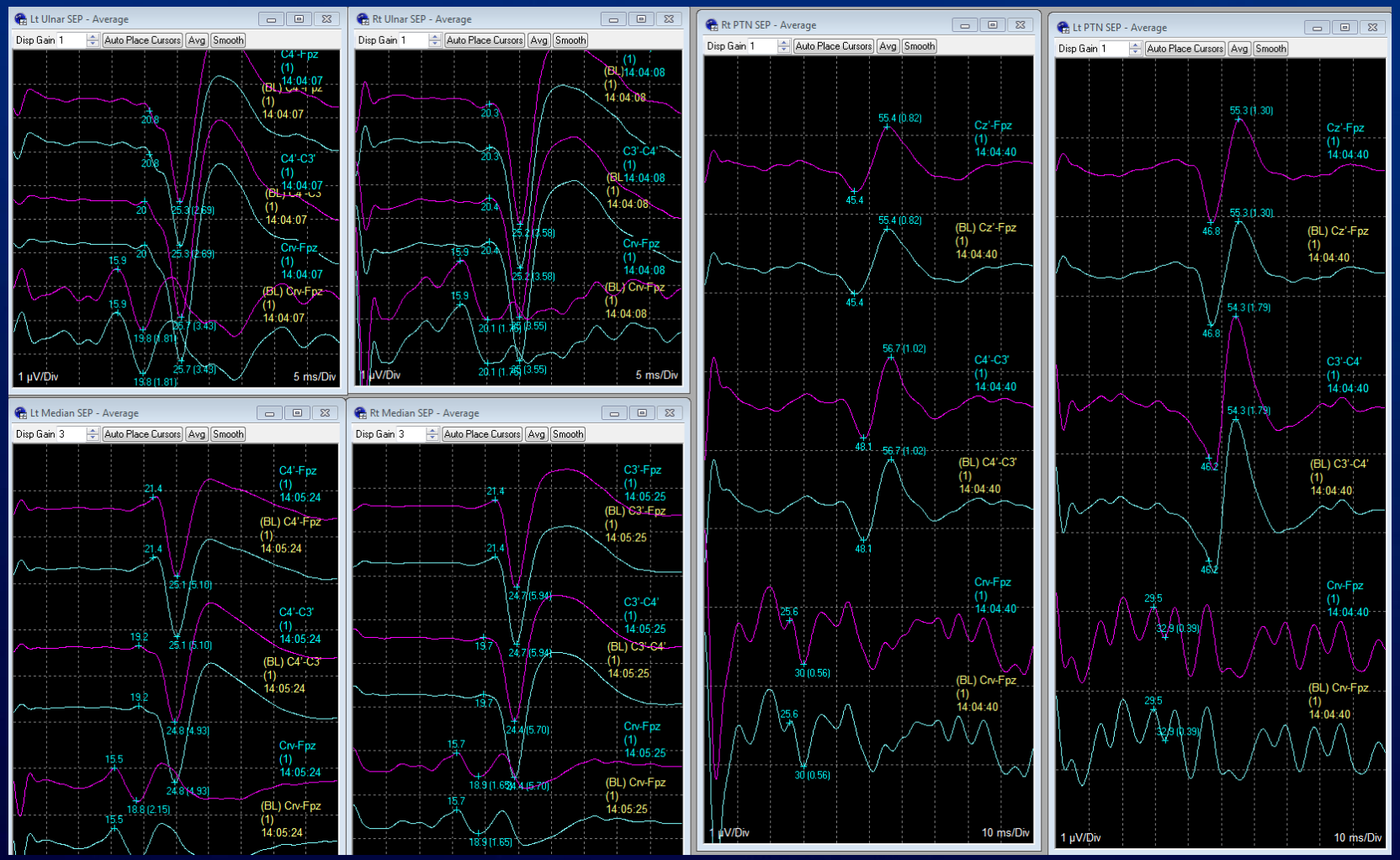
Cervical MRI



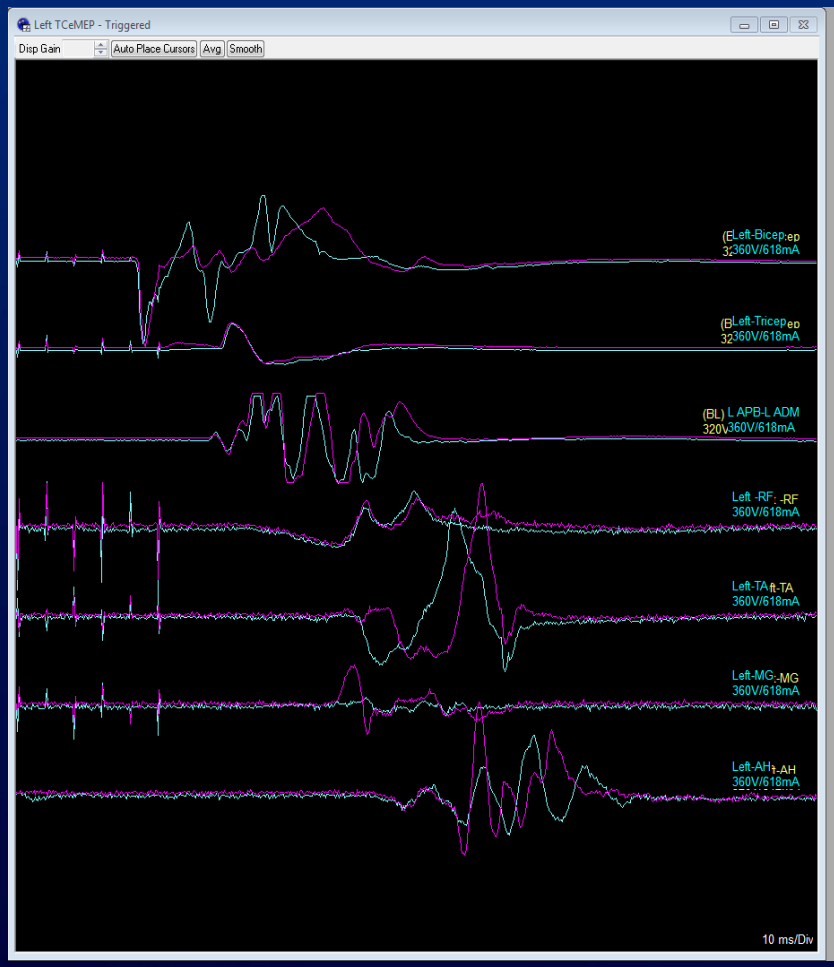
Thoracic Lesion

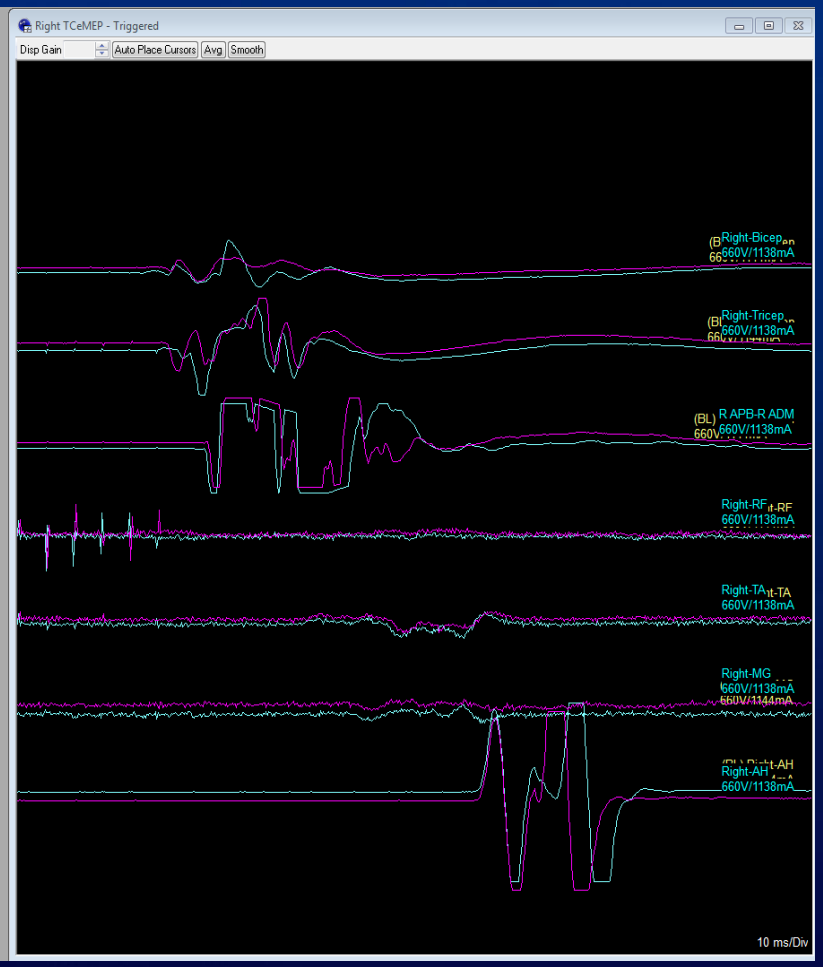


Baselines SEPs



Baseline MEPs





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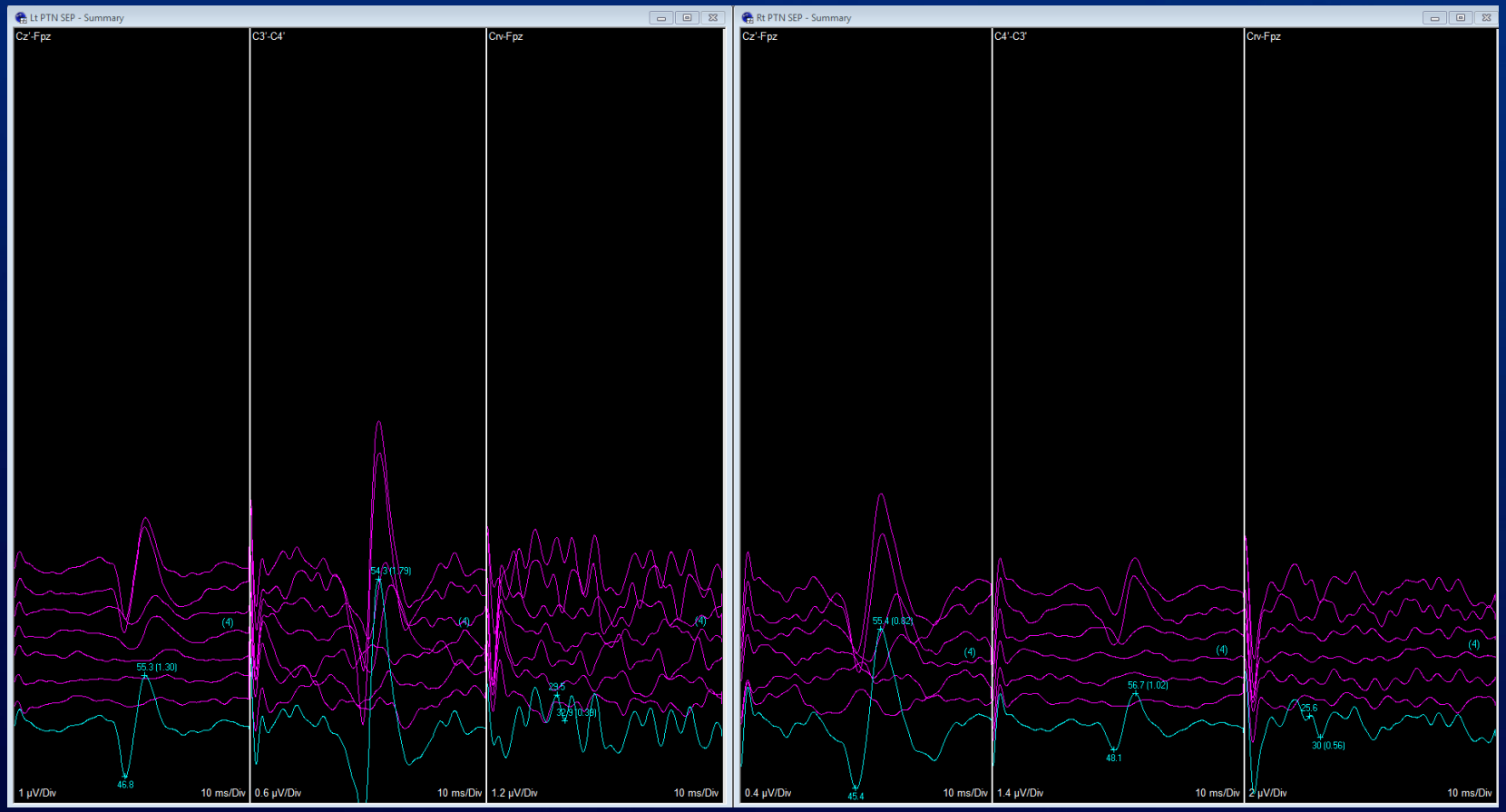
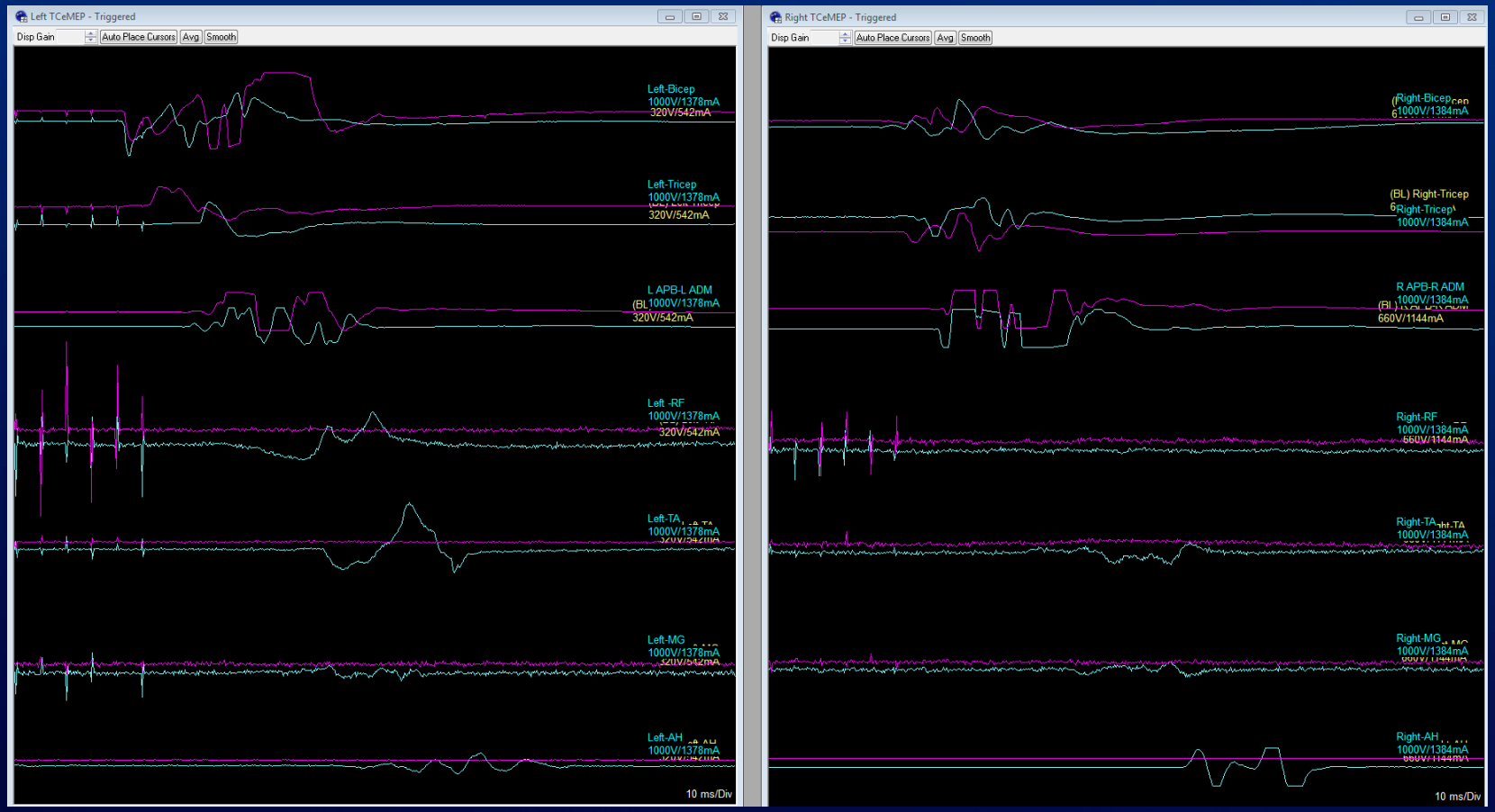
Unable to run MEPs due to muscle relaxant for opening. Only SEPs monitored with runs between Bovie's use. Tibial SEP change.



MAYO CLINIC

First MEPs after paralytic wore off, maximal stimulation



Sequence of events:

- Decline of tibial SEPs : 14:37
- Loss of tibial SEPs : 14:45
- Unable to check MEPs due to muscle relaxant on board
- Thecal sac open : 15:14 PM
- Loss of MEPs : 15:15 PM?

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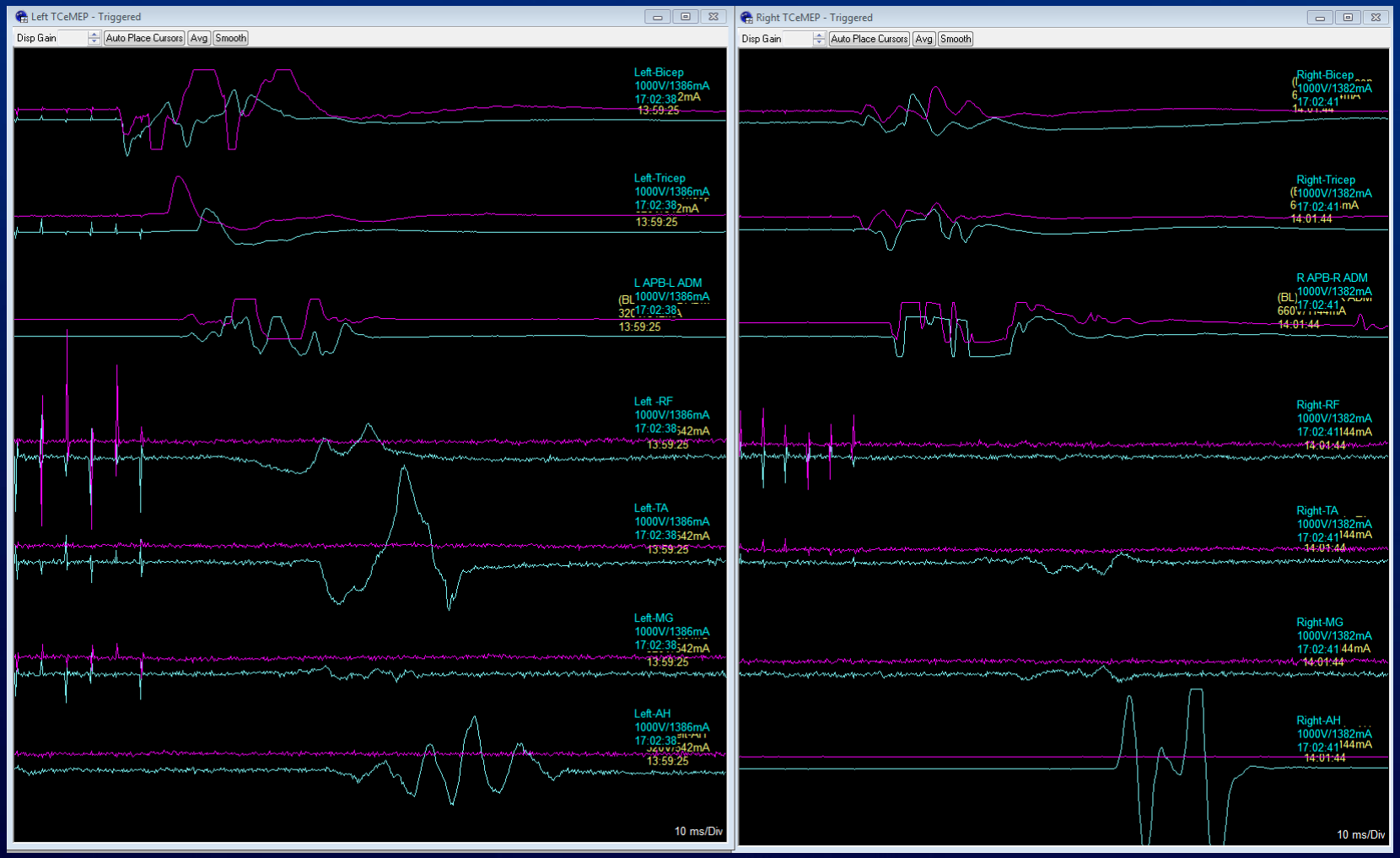
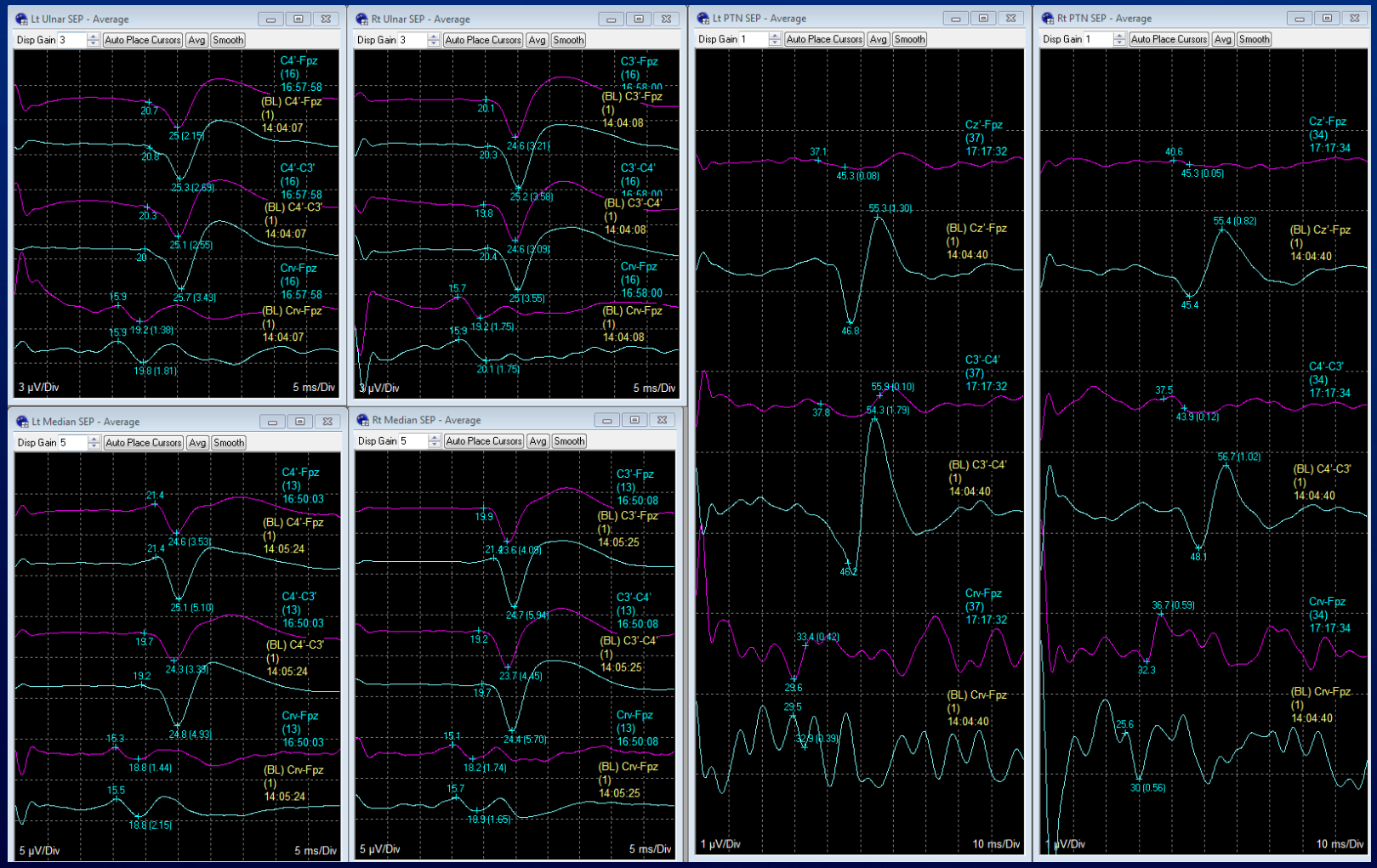
End of case MEPs



MAYO CLINIC

End of case SEPs



What has happened?

- Abrupt change
- Loss of both sensory and motor responses
- Low BP during opening

- Patient woke up with paraplegia

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Take Home Message about Muscle Relaxants Use in NIOM

- Avoid and reverse NMB before critical steps to avoid false negative free run EMG and/or false positive MEP changes
- Avoid with baselines and positioning
- Avoid with triggered EMG

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Benzodiazepines

- Amnesic, sedative GABAa agonists
- Useful in reducing hallucinatory effect of ketamine

- SEP: Subcorticals unaffected
- SEP: Cortical mildly attenuated
- MEP: May inhibit MEPs at high doses

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Opioids

- Analgesics
- SEP:
  - Modest cortical attenuation at high doses

    Kalkman C. Journal of Cardiothoracic Anesthesia, 1988; 758-764

- MEPs D and I waves unaffected
- MEP CMAP – abolished at high doses

  Thees C. J Neurosurg Anesthesiol1999; 112-118

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NIOM Anesthesia Main Principles

- Avoid boluses, prefer continuous infusions
- Avoid muscle relaxants for baseline, positioning and post-positioning MEPs
- Avoid muscle relaxants for free and triggered EMG
- Avoid inhalationals for SEPs and MEPs
- Inhalationals are the preferred choice for CEA due to burst suppression with propofol
- TIVA (propofol and opiod) are the preferred choice for spine monitoring with MEPs and SEPs
- Titrate to strike a balance

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Conclusions

A combination of neurophysiologic procedures selected on an individual basis and a multidisciplinary approach is necessary

The exact modalities/techniques in combination with the anesthetic choice (used in NIOM) are prioritized on a case-by-case scenario

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Thank you

Questions & Discussion