Outline

• Alzheimer’s Disease
• Epilepsy
• Parkinson’s Disease
• Multiple Sclerosis
• Huntington’s Disease
Alzheimer’s Disease

4.5 million in US

Neurofibrillary tangles

Amyloid plaques

Healthy

Alzheimer’s

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Dementia

- memory
- concentration
- judgment
- decision
- mood

- history?
- consent?
- cooperative?
- delirium?
Post-op Delirium

Risk Factors
- Age >65
- Dementia
- Functional impairment
- # comorbidities
- Substance abuse

Medication induced
1. benzodiazepines
2. morphine
3. anti-cholinergics

Rx: haloperidol 1-2 mg (PO/IM/IV)

Ribinson, Clin Interv Aging 2008
Medications

- Memantine
- Donepezil
- Galantamine
- Rivastigmine
- Tacrine (discontinued in U.S.)
Cholinesterase Inhibitors

- Prolonged response to succinylcholine.
- Resistance to non-depolarizing NMB’s.
- Vagotonic effects of SA & AV node:
  - Bradycardia, syncope
- Bronchoconstriction
- Cholinergic crisis
Effect of Anesthesia?

  - Enhanced beta-amyloid, cytotoxicity.
- Planel (2007)
  - Abnormally hyperphosphorylated tau.
- Perucho (2010)
  - Increased beta-amyloid aggregates.
Effect of Anesthesia?

No correlation:
2. Gasparini (2002) Italy

Possible correlation:
1. Bufill (2009) Spain

Need prospective data
Key Points

• Difficult to obtain H&P, consent, etc.
• High risk of developing post-op delirium.
  – Avoid benzodiazepines.
• Cholinesterase inhibitors have many potential interactions and side effects.
• No definitive association between anesthesia and developing Alzheimer’s disease.
Epilepsy

Recurrent, unprovoked seizures.

- 2 million in U.S.
- 1 in 25 people

Various elective & emergency surgeries
Epilepsy surgery
Treatment of status epilepticus
1. **Minimize perioperative seizures.**
   - Avoid disruptions in anti-epileptics.
   - Avoid pro-convulsant anesthetics.

2. **Drug interactions of anti-epileptics.**
   - Cytochrome P450 enzyme induction.
   - Decreased effectiveness of drugs.
It’s Complicated!

- Pro-convulsant vs. anti-convulsant.
- Abnormal movements are common.
- Epileptics seize.

Voss, Anesth Analg 2008
Anesthetics and Seizures

Proconvulsant
- Enflurane
- Sevoflurane
- Etomidate

Anticonvulsant
- Isoflurane
- Desflurane
- Propofol
- Benzodiazepines
- Thiopental
- Ketamine
- Nitrous oxide
Interaction of Anti-epileptics

**CP450 Inducers**
- Phenytoin
- Carbamazepine
- Phenobarbital
- Primadone

↓ plasma concentration
- NMB’s
- Opiates
- Benzodiazepines
- Dexamethasone
- Amiodarone
- Beta Blockers
Key Points

- Avoid disruptions in anti-epileptics.
- Avoid etomidate and sevoflurane.
- CP450 enzyme inducers:
  - phenytoin
  - carbamazepine
  - phenobarbital
  - primadone

Tolerant to non-depolarizing NMB’s and opiates.
Parkinson’s Disease

• Degenerative disease of CNS
  – Loss of dopamine generating cells
• 1 million in U.S.
• M>F, increases with age.

Emergent and elective
Deep brain stimulator
Generator change
Case

- 75 yo male: deep brain stimulator.

PMH
- Parkinson’s
- Anxiety/depression
- Hypertension
- Heartburn
- PONV

Medications
- Carbidopa-levodopa
- Selegeline
- Citalopram
- Buspirone
- Benazepril
- Omeprazole
Carbidopa-levodopa

dosing interruptions

“off drug state”

Rebound worsening of motor symptoms and mental state

-Respiration
-Aspiration
-NMS*
Case

- 75 yo male: deep brain stimulator.

PMH
- Parkinson’s
- Anxiety/depression
- Hypertension
- Heartburn
- h/o PONV

Medications
- Carbidopa-levodopa
- Selegiline
- Citalopram
- Buspirone
- Benazepril
- omeprazole
Selegiline, rasagiline

- Monoamine oxidase inhibitor (MAOI)
  (A): Dopamine, Epi, NE, tyramine, serotonin
  (B): Dopamine
- No dietary restrictions.
- Hypertensive crisis?
- Serotonin toxicity?
  - selegeline + antidepressant
  - 2 patients (out of 4500) serious symptoms

Richard, Neurology 1997
Exacerbation of symptoms?

prochlorperazine
ondansetron
promethazine
metoclopramide
droperidol
scopolamine
# Dopamine Antagonism

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Key Points

• Avoid interruptions of carbidopa-levodopa.
  “off drug state,” NMS.

• Selegiline, rasagline: 
  selective MAO-B inhibitor.

• Caution with anti-emetics:
  - droperidol, - prochlorperazine
  - promethazine - metoclopramide
Multiple Sclerosis

- Demyelinated plaques
- Multifactorial etiology
- 400,000 in U.S.
- F > M, 20-50 yrs of age

Various elective and emergency surgeries
- Labor and delivery
- Deep brain stimulator, intrathecal pump

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Multiple Sclerosis

- airway → aspiration
- respiratory → hypoxia
- cardiac → dysrhythmia
- muscle → hyperkalemia
Hyperthermia

• 1890: amblyopia after exercise.
• 1960’s: hyperthermia was the culprit.
  – Conduction blockade.
  – Worsening, or new neurological deficit.
  – Usually reversible.
• Occurs with even a 1°C increase.

***Monitor temp, treat aggressively.***
Effect of Anesthesia?

- "stress" → exacerbation
- All anesthetic techniques have been implicated.
- General anesthesia is better than neuraxial techniques.
- Epidural is better than spinal.
- Data?
Effect of Anesthesia?

• 1998: Pregnancy in MS (PRIMS) study
  – Epidural analgesia did not increase the rate of relapse or worsen the progression of the disease.

• 2006: Neuraxial anesthesia with CNS disease.
  – No new or worsening postop deficit.
  – “evidence that it worsens it is lacking, if there is any increased risk, likely minimal”.

Modifiable Factors

No association
- Surgery
- Anesthesia
- Vaccinations
- Epidural for labor
- Physical trauma

Strong association
- Infections
- Pregnancy
  - 3rd trimester
- Stressful life event
- Smoking

D’hooghe Multiple Sclerosis 2010
Key Points

• Advanced disease increases risk.
  – Aspiration, respiratory issues.

• Avoid hyperthermia.
  – Monitoring and treatment.

• Effect of anesthesia is minimal.
  – General anesthesia---safe.
  – Epidural anesthesia---safe.
  – Need more data for spinal.
Huntington’s Disease

- Degenerative brain disease
- Autosomal dominant
- 30,000 in U.S.
- F=M, 40 yrs of age

Various elective and emergency
- Feeding tube
- Dental procedures
Symptom Triad

- Symptom 1
- Symptom 2
- Symptom 3
Treatment

Symptoms

- Antipsychotics
- Antidepressant
- Tranquilizers
Tetrabenazine

• Only FDA approved drug for Chorea.

• Inhibits VMAT2

• NMS: droperidol, metoclopramide

• Prolongs the QT interval

Dopamine
norepi
serotonin
Complications?

- 23 case reports (1960-2010)
  - Prolonged apnea
  - Prolonged recovery: STP, BZD
  - Tonic/clonic movements
  - Shivers, fever

sucinylcholine, thiopental, benzodiazepines
J. E. Kivela et al. A & A 2010:

- 20 yrs experience at Mayo Clinic.
- 11 pt’s (17 general anesthetics)
  - Normal response to NMB’s, induction and maintenance anesthetics.
  - Normal recovery times, no serious post-op complications.

Unremarkable anesthetic course
Key Points

- Symptoms:
  - Difficult IV, regional anesthesia
  - Informed consent?
  - Cooperation for MAC?
  - Dysphagia: RSI

- Tetrabenazine: NMS, QTc

- There is no “best” anesthetic.
Summary

1. Symptoms have many pertinent anesthetic implications.  
   (Airway, respiratory, cognitive issues)

2. Avoid interruptions of regular meds.  
   (Anti-epileptics, Carbidopa/levodopa)

3. Medications can have significant interactions and side effects.  
   - Cholinesterase inhibitors  
   - CP 450 inducers  
   - Dopamine antagonist
Summary

Alzheimer’s disease:
- Positive neuropathologic animal data
- Inconsistent human data

Epilepsy:
- Avoid sevoflurane and etomidate.

Multiple Sclerosis:
- GA and epidurals appear to be safe with minimal risk.
- More data on spinal anesthesia.


References


