Considerations for Surgical Treatment for Adult Epilepsy

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Case Study #1

M.A. is 24 y/o woman with complex partial seizures that began at age 12. She was treated with carbamezepine and lamotrigine but never able to achieve complete seizure control. When referred, she continued to have 2-3 complex partial seizures per month. She was interested in attending graduate school and engaged to be married.
Case study #2

H.K. - 56 y/o man with a history of epilepsy since age 7 and a history of a febrile seizure as an infant. Seizures were controlled with medications for 20 years, but then he began having breakthrough complex partial seizures with loss of awareness. He trained as a medic, but has been on disability and unable to work for many years. Between age 27 and 56, he was cycled through most of the available anti-seizure medications and was on three medications when referred for epilepsy monitoring. Seizure frequency is 3-4 seizures per month.
Overview

• When should surgical treatment options for epilepsy be considered?

• What does the surgical evaluation for epilepsy involve?

• Who is likely to benefit from epilepsy surgery?
All patients with a diagnosis of intractable (drug-resistant) epilepsy were considered for referral for a neurologic evaluation of appropriateness for surgical therapy and the consideration was documented in the medical record within the past three years.
What is drug-resistant epilepsy?

- A convenient historical definition was seizures refractory to all approved anti-seizure medications but with the number of choices now available this would now take a lifetime.

- The current definition is based on studies of epilepsy response to treatment with anti-seizure medications.
Anti-seizure medication response – Prospective Study

Previously Untreated Epilepsy Patients (n=470)

- Seizure-free with 1st drug: 36%
- Seizure-free with 2nd or 3rd drug: 14%
- Seizure-free with multiple drugs: 3%
- Pharmacoresistant epilepsy: 47%

What about newer AEDs?

- 16% of drug introductions led to seizure freedom for 12 months
- Longer duration of epilepsy and past treatment with more than 5 drugs was also associated with lower likelihood of seizure freedom

Definition of drug-resistant epilepsy

Failure of adequate trials of two tolerated, appropriately chosen, and appropriately used anti-seizure drug regimens to achieve freedom from seizures.
Natural History of Epilepsy

- 2/3 of individuals controlled on anti-seizure medications
- 1/3 of individuals drug-resistant
- Relapse and remission rate around 4% per year
- With drug-resistant epilepsy, sudden unexpected death in epilepsy (SUDEP) risk is 0.5 -1% per year

*Berg et al., Neurology, 2003; 60(2): 186-190.*
How do surgical options compare to medical therapy in drug-resistant epilepsy?
Surgical vs. Medical Therapy

• 80 patients with temporal lobe epilepsy, randomized to best medical treatment while surgery is delayed one year (40 patients) versus immediate evaluation then surgery (40 patients - 36 operated)

• Free of seizures affecting consciousness at one year:
  – Medical group: 8%
  – Surgical group: 58% (64% of operated pts)  P<0.001

Wiebe et al., NEJM 2001;345:311-8.
Epilepsy Presurgical Evaluation

• **Purpose:** Localization of the seizure onset zone and define it’s relationship to primary language, motor, sensory, and memory regions.

• **Evaluate the potential benefit vs. risk of surgical treatment**
Presurgical Evaluation
History and Exam

• History – identify potential causative factors for epilepsy
• Seizure descriptions
  – description of aura
  – focal features during seizure progression
  – automatisms
  – language manifestations
  – postictal manifestations
• Physical examination: focal/generalized deficits
Presurgical Evaluation: MRI

- Identify structural lesions that cause seizures
  - tumors
  - cavernous angiomas
  - arteriovenous malformations
  - hippocampal sclerosis
  - encephalomalacia: traumatic brain injury, stroke
  - developmental malformations: focal cortical dysplasia, heterotopias, other
Mesial temporal lobe sclerosis
Cavernous Angioma

T2-weighted

FLAIR
Left frontal low grade tumor
Right temporal low grade tumor
Old (intrauterine) stroke
Developmental abnormality
Presurgical evaluation: Video-EEG monitoring

- Inpatient monitoring for several days.
- Anti-seizure medications are withdrawn.
- Seizures and interictal epileptiform activity are recorded to try to define the seizure onset zone.
- Typically like to see at least 4 seizures for localization.
Neuropsychological Testing

- Series of tests of attention, memory (verbal and visual), problem solving skills, overall cognitive functioning.
- Assesses functioning of different regions and sides of the brain to identify brain regions that are not functioning optimally.
- Helps with decision making for surgery – often brain regions where seizures are starting are not functioning optimally.
- May provide predictive information regarding risks of surgery.
Presurgical evaluation: PET imaging

• Short acting radiotracer (18- FDG) is injected intravenously and is taken up by cells in the brain

• PET scan images brain based on level of glucose uptake – a measure of brain metabolism

• Focal regions of low uptake correlate highly with seizure onset zone as identified by intracranial monitoring
Standard presurgical evaluation

- **Inpatient Video-EEG monitoring**
  - Interictal and ictal discharges with mesial temporal pattern

- **MRI**
  - Hippocampal atrophy
  - Increased signal

- **PET**
  - Interictal right temporal hypometabolism

- **Neuropsychological testing**
  - Impaired visual memory suggestive of right temporal dysfunction
Multidisciplinary Epilepsy Surgery Conference

- All test results are presented and reviewed at a conference attended by neurologists, neurosurgeons, and neuropsychologists to make an epilepsy surgery recommendation.
In Wada test an anesthetic agent (sodium amobarbital) is infused to each brain hemisphere sequentially to evaluate the location of language and memory.

- Injection of the epileptogenic side without deficit predicts surgical safety.
Ictal SPECT

• Short acting radioactive tracer is injected at seizure onset
• Tracer is distributed with blood flow and taken up by cells in the brain in proportion to blood flow.
• Early injections most likely to be helpful.
• Injections with simple partial seizures uninformative in ~40% of cases.
• Injections with secondary generalization potentially misleading.
• Subtraction from interictal SPECT and coregistration with MRI make studies more useful
Presurgical evaluation: MEG
Adult Epilepsy Surgery Types

• Temporal lobectomy
  – Standard
  – Selective amygdalohippocampectomy

• Lesionectomy

• Intracranial EEG monitoring
  – Depth electrode implantation
  – Subdural electrode grid implantation
  – Goal is tailored temporal or extratemporal resection

• Palliation/disconnection
  – Callosotomy
  – Multiple subpial transections (MST)
  – Vagal nerve stimulation (VNS)
Standard Temporal Lobectomy
Selective Amygdalohippocampectomy

Approach corridor
Selective Amygdalohippocampectomy

- Extent of resection
  - Medial amygdala
  - Hippocampus
  - Parahippocampal gyrus

- Outcome not statistically different than standard anterior temporal lobectomy

Intracranial EEG monitoring

- Seizure onset zone is well lateralized but not well localized

- Bitemporal independent seizure onset zones?

- Epileptogenic zone may overlap with eloquent cortex (example: language or motor)

- Non-lesional epilepsy
  - For better localization of seizure onset zone in the absence of an epileptogenic lesion
Invasive EEG techniques

• Subdural grid electrodes
  – For better localization of the seizure onset zone
  – Stimulation mapping of brain function

• Depth electrodes
  – For assessment of deep structures such as the mesial temporal lobes
Intracranial EEG: subdural electrodes
Functional mapping of eloquent cortex
Which individuals with epilepsy are most likely to benefit from surgery?
Unilateral hippocampal sclerosis
Lesional Epilepsy

- Clear lesion associated with seizure type
- Epileptic zone congruent with the lesion
- Resection of lesion and perilesional tissue
Epilepsy Surgery Risks

• Visual field deficits (temporal lobe surgery)
• Memory decline – usually mild
• Post-operative depression – most improve
• Surgical complications (<4%)
  – Stroke
  – Infection
Outcome after epilepsy surgery

- **Engel et al., Neurology 2003; 60: 538-47.** Meta-analysis of 21 studies with 1769 patients with anteromesial temporal lobe surgery with 2-5 year follow-up.
  - 65% of patients free of disabling seizures,
  - 21% improved,
  - 14% not improved

- **Tellez-Zenteno et al., Epil Res 2010; 89:310-18:** Meta-analysis for outcomes in lesional vs. non-lesional epilepsy
  - Temporal: 69% seizure free for lesional vs. 45% for non-lesional
  - Extratemporal: 66% seizure free for lesional vs. 34% for non-lesional
Post-surgical quality of life improvement

Prospective multicenter cohort study of 396 individuals who had undergone epilepsy surgery for 2 years

• Health-related QOL after epilepsy surgery improves at 6 months regardless of seizure outcome, but continued improvement at 2 years seen in those who are seizure free.
• At 2 years, 76% said would definitely have surgery again, additional 12% said probably
• 79% said that surgery had a strong or very strong positive impact
  – correlated with seizure freedom, seizure reduction, and employment gains

Spencer et al., Ann Neurol 2007; 62: 327-334
Chin et al., Neurology 2006;66:1882-1887
Case Study #1

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PET imaging
Neuropsychological Testing and Wada

- Suggestive of left temporal and parietal dysfunction based on performance on language tasks

- WADA showed right temporal lobe was dominant for memory
Case study #1 - continued

She underwent a left temporal amygdalo-hippocampectomy and lesionectomy (pathology consistent with dysplastic cortex). She has been free of all but seizure auras since surgery 6 years ago. She tapered completely off of antiepileptic medications 3 years after the surgery. She is now married and has had a son from an uncomplicated pregnancy after tapering off antiepileptic medications. She is driving again, has completed her a graduate degree and is now working as a teacher.
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Case study #2 - continued

During EMU admission, he had 11 typical complex partial seizures all with left temporal onset. MRI showed clear left mesial temporal sclerosis. Based on this, he would likely be an excellent surgical candidate with a high chance for seizure freedom. This was discussed with him and his response was:

“If we had known about this earlier in life, I might have considered this... but the Lord has brought me through this far...”
Summary

• Drug-resistant epilepsy can and should be identified early based on lack of response to adequate trials of two anti-seizure medications

• Epilepsy surgery has a high success rate in eliminating disabling seizures and improving quality of life

• Individuals with mesial temporal sclerosis or lesional epilepsy have the highest rate of post-surgical seizure freedom