Functional Neurosurgeon

- “Neurosurgery intended to improve function”
- Surgery for:
  - Pain
  - Movement disorders
  - Epilepsy
  - Behavioral disorders (?)
Functional and Stereotactic Neurosurgery

- 1946: Stereotaxis
  - "Touching a point in space"
  - Speigel and Wycis (Temple U., Philadelphia)
- Parkinson Disease (tremor)
- Pain
- "Emotional disorders"
- 1950-1968: Thalamotomy vs pallidotomy
- 1964: Microelectrode recording
- 1968 – Levodopa era
- Stereotactic surgery almost disappears

How are DBS electrodes implanted?

Stereotactic Frame
Pallidotomy

Brain Stimulation
- Pain
- Movement disorders
- Epilepsy
- Behavioral disorders
- Future indications

DBS: Pain
- 1954-60 – Olds, Heath, Pool
  - Septal region (“pleasure centers”)
- 1960 – Mazars
  - Thalamic (VPL) stimulation for pain
- 1969 – Reynolds
  - PAG stimulation in rats produces analgesia
- 1976-78 - Richardson and Akil
  - DBS for pain
    - 1977-78 - Adams
    - 1977-78 - Henschuck
    - 1986 - Young
DBS for Pain
• Case series (no RCT)
  – Does not meet contemporary standards of evidence
• No FDA approved pain indication

DBS: Movement Disorders
• 1982 – Siegfried and Lipputz – DBS for tremor
  – Patient implanted for pain in thalamus
  – Tremor improved
• 1987 – Benebid (U. Grenoble)
• 1990 – First US DBS (OHSU)
• 1999 – First RCT of DBS (OHSU)
• 2009 – DBS v BMT NIH/VA trial
First US DBS

First DBS
DBS: Implant Procedures

DBS for Parkinson Disease

Pre-operative/off medication

Pre-operative/on medication
DBS for Parkinson Disease

Post-operative/on medication

DBS: Movement Disorders

- DBS for PD was superior to best medical therapy
  - Improved on-time, motor function, and quality of life
  - Both older and younger patients
  - Both early and later stages of PD
- DBS for PD works in both STN and GPi
  - Lower levodopa requirement in STN patients
  - Visual processing worse with STN stimulation
  - Depression worsened with STN stimulation and improved with GPi stimulation

Bilateral Deep Brain Stimulation vs Best Medical Therapy for Patients with Advanced Parkinson's Disease: A Randomized Controlled Trial. JAMA 301:63-73, 2009
Pallidal versus Subthalamus Deep-Brain Stimulation for Parkinson’s Disease. NEJM 362: 2077-2091, 2010

DBS: Behavioral Disorders

- Depression
- Obsessive Compulsive Disorder
- Tourette’s Syndrome
DBS: Depression Studies

- 21 patients (pilot study)
  - Toronto, Montreal, Vancouver
- Open label trial [not randomized]
- 50% reduction in depression rating
  - 1 mo – 57%
  - 6 mo – 48%
  - 12 mo – 29%
- SAE: 8 patients [38%] had 10 SAEs
DBS: Obsessive Compulsive Disorders
• All small case series
  – Not randomized
• “…reveal clinically significant symptom reductions and functional improvement in about two-thirds of patients”

DBS: Epilepsy
• SANTE trial (2010)
  – Stimulation of anterior nucleus thalamus
    • 110 patients
    • 3 month blinded
      – 40.4% on DBS therapy
      – 14.5% placebo
    • Unblinded stimulation
      – 56% reduction of seizures from baseline @ 25 months
      – 56% responders @ 75% @ 27 months
    • 30% SAE
      – 6 deaths
      – 14 suicidality
      – 10 infections
      – 6 sternal fractures
      – 4 hemorrhages
  – FDA approval is pending
    • Approved in Europe and Canada

DBS: Epilepsy
• Neuropace RNS trial (2009)
  – Hippocampus stimulation + cortical
    • 1 month baseline
    • 3 months randomized blinded trial
      – -37.9% on therapy
      – -17.3% placebo
    • SAE 18.3%
  – Now FDA approved
Brain Stimulation

- Pain
  - Not proven, not approved, rarely used
- Movement disorders
  - Proven, approved, used widely
- Epilepsy
  - Proven, approved, early stage of use
- Behavioral disorders
  - Not proven, not under FDA review currently

DBS: The Future
Bioethical Considerations

- DBS is less controversial than:
  - Stem cell research
  - Fetal tissue, abortion
  - Animal testing
- However:
  - Legacy of psychosurgery
  - DBS is still poorly understood therapy

- Hailed as a treatment for many diseases!

Bioethical Considerations

- Current indications….
  - Parkinson disease, tremor
  - Epilepsy
  - Pain
- …are not primarily psychological problems
- Newer developments in DBS may blur that distinction
- Does science have the obligation or right to alter someone’s behavior and call it therapeutic?
- The public is rightfully distrustful of therapies whose primary goal is to change behavior

Brain Stimulation: Future

- Probable
  - Epilepsy
  - Obsessive compulsive disorder
  - Depression
- Possible
  - Pain
  - Tinnitus
  - Drug Addiction
  - Obesity
  - Alzheimer’s disease
Entorhinal Cortex Stimulation

DBS: The Future?

- Alzheimer’s Disease
  - 5.4 million Americans now living with AD
  - 1/8 older Americans
  - 6th leading cause of death
  - Cannot be prevented, cured or slowed
  - 2012: $200 billion health care spending
    - 2050: $1.1 trillion annually

Brown adipose tissue (BAT)

Medial hypothalamus

Cost exposure

Brown adipose tissue (BAT)
Future of DBS?

- Alzheimer’s Disease
  - 5.4 million Americans now living with AD
  - 1/8 older Americans
  - 6th leading cause of death
  - Cannot be prevented, cured or slowed
  - 2012: $200 billion health care spending
  - 2050: $1.1 trillion

- Obesity
  - 2030
  - 42% of Americans
  - $550 billion health care spending