DBS: PATIENT SELECTION AND TREATMENT OPTIONS

Lin Zhang, MD, PhD
Medical Director, DBS Program
Department of Neurology
UCDavis School of Medicine
DISCLOSURE

• NOTHING...BUT
OBJECTIVES

• Describe the Approved Indications and Patient Selection Process for DBS surgery

• Introduce technical options of DBS

• Provide an Overview of future indications for DBS surgery
BRIEF HISTORY

• 1930s: Basal ganglia targeted for neuromodulation
• 1950: Pallidotomy was an accepted procedure for treatment of PD
• 1952: Irving Cooper (1922-1985) first tried ACA ligation to treat Parkinsonism
• Late 1980s-early 1990s: Limitation of dopaminergic therapy led to a resurgence of new surgical techniques directed at basal ganglia targets
• 1993: high frequency stimulation of STN was introduced in treatment of advanced PD
OVERVIEW

- Offers hope to severely impaired patients when symptoms are intractable despite optimal medication and other available therapies
- Over two decades of safety
- Over 100,000 stimulators implanted worldwide as of December, 2012
- Over 3,500 published articles on DBS
- With proper patient selection, there is improvement seen with: standard scales, quality of life, co-morbid conditions, medication intake, and chronic care costs
DBS: A TREATMENT OF MOVEMENT DISORDERS

- Unlike ablative procedures, DBS is reversible and adjustable.
- Consider safe and effective for management of the motor symptoms of these disorders
- Potential complications include ICH, infections, and hardware-related complications
- Proper patient selection is the key to the success of the surgery
APPROVED INDICATIONS

Essential Tremor:
• FDA approved in 1997

Parkinson’s disease:
• FDA approved in 2002

Dystonia:
• FDA approved (HDE) in 2003

Obsessive Compulsive Disorder:
• FDA approved (HDE) in 2009
HARDWARE AND TARGETS

- DBS devices have three components: the DBS lead, the Implantable Pulse Generator (IPG), and an extension cable connecting the two.
- Can have b/l or u/l lead and u/l or b/l IPG.
- Can have nonrechargeable or rechargeable IPG.
The components of an implantable deep brain stimulation system.
PATIENT SELECTION

- The multidisciplinary team include: Movement disorder neurologist, a subspecialized neurosurgeon, a neuropsychologist
- Selection process focuses on: clinical assessment, cognitive risks, outcome analysis, patient expectations
- The goal is to find ideal patients: where individual benefit outweighs the risk of surgery
INCLUSION CRITERIA

- PD: advanced stage with motor complications
- Tremor: interferes with ADLs AND medications are ineffective and/or cause intolerable side effects
- Dystonia: at least 7 yo, chronic primary dystonia, unsuccessful medication management
PRE-OP EVALUATION

- Detailed neurologic evaluation
  - On-Off Testing to determine the extent of dopaminergic responsiveness

- Neuropsychological evaluation
  - Determination of cognitive status
  - Assessment of mood and psychotic symptoms

- Neurosurgical consultation
NEUROPSYCHOLOGICAL ASSESSMENT

- Dementia is screened using MMSE or MoCA
- Assessment of general cognitive functioning: such as:
  - Executive functioning,
  - Short and long term memory
  - Visual spatial and language function
- Identification of pattern of dementia: ?DLBD, ?PSP, and AD
- Rejection based on: MDRS 2 or more SD beyond age-adjusted mean normal score.
NEUROPSYCHOLOGICAL ASSESSMENT

- Screen for depression, anxiety, and psychosis
- Patient with mood disorders are generally excluded
- Following DBS surgery, patients can have hallucinations, psychosis, mania, and impulsivity.
INCLUSION CRITERIA FOR PD DBS SURGERY

- Diagnosis of Idiopathic Parkinson’s Disease
- Disabling or troubling motor symptoms despite optimized pharmacological treatment
- Robust motor response to levodopa (>30% improvement on UPDRS III)
- Clear understanding of risks and realistic expectations
EXCLUSION CRITERIA FOR PD DBS SURGERY

- Serious surgical co-morbidities
- Poorly controlled psychiatric illness, including anxiety and mood disorder
- Dementia
- Preop MRI with extensive WM changes or severe cerebral atrophy
DETERMINATION OF ELIGIBILITY FOR ET

- Confirmation of IET diagnosis
  - Core criteria: Bilaterality, absence of cogwheeling, absence of dystonia
  - Secondary criteria: long duration, positive family history, and beneficial response to alcohol

- Documentation of mediation responsiveness

- Red Flags: U/L tremor, gait disturbance, Focal tremor, isolated head tremor, sudden onset.
TARGET CHOICE

Vim Thalamus (VIM): Essential Tremor

Subthalamic Nucleus (STN): Parkinson’s disease and Dystonia

Globus Pallidus (GPi): Parkinson’s disease and Dystonia
TARGET CHOICE

IC = internal capsule
STN = subthalamic nucleus
ML = medial lemniscus
RN = red nucleus
HOW IS THE SURGERY DONE?
PRE-OPERATIVE STAGE

- Locate Target Brain Areas;
- Apply Stereotactic Frame;
- MRI, CT or Ventriculography;
- Stereotactic Atlas on Stealth station
Implantation of electrode and Test Stimulation

1. Electrode has 4 contacts at its distal end,
2. the effects of stimulation from each combination of 2 contacts or monopolarly from each contact are assessed
3. Determine best contact(s) to use to obtain optimal therapeutic benefit
Electrode-Stimulator Connection

- Electrode-> extension (passed underskin to chest) -> Chest: Battery-operated stimulator
- Patient turns stimulator “on” and “off” by passing magnet over the skin overlying stimulator
- Typical stimulator settings: 2-3V, 90us and 130-185Hz
ELECTRODE-STIMULATOR CONNECTION

- Stimulator parameters adjusted via a computer-controlled probe placed over stimulator
- Pulse generator can be adjusted post-operatively by telemetry: (1) electrode configuration, (2) Voltage amplitude, (3) Pulse width, and (4) Frequency

- **Pulse Width** (sec) - duration of each stimulus
- **Rate** (Hz) - number of pulses per second
- **Amplitude** (Volts) - intensity of stimulation
ADVANTAGES OF DBS

- Avoid adverse side effects associated with lesioning procedures
- Does not require deliberate destruction of brain regions
- Effects of stimulation therapy are reversible
  - Due to reversibility, does not preclude use of future therapies
- Can change stimulation parameters to optimize clinical benefit
- Can be safely performed bilaterally (in contrast to ablative procedures)
- May be the only effective treatment of levodopa-induced dyskinesias
- The beneficial changes are long-lasting
COMPLICATIONS OF DBS

- Surgical complications
  - ICH, infection, lead misplacement,

- Hardware complications
  - Lead migration, lead failure, pain, skin erosion

- Stimulation-related complications
  - Unintended clinical effects, dyskinesia, worsening axial symptoms (freezing, balance, and gait disturbance), speech disturbance, paresthesia, diplopia, and weight gain
DBS: STIMULATION-PRODUCED ANALGESIA

- DBS is NOT FDA approved for pain and represents an off-label use of the implanted device
STIMULATION-PRODUCED ANALGESIA

• Reynolds, 1969: Science
  • Electrical stimulation of rat midbrain results in profound analgesia without concurrent administration of analgesic drugs
• Richardson, 1973
  • First published report of PAG-PVG stimulation in humans
DBS PAIN TARGETS

• PVG and PAG
  • Activation of endogenous opiate systems
  • Descending modulatory pathways
  • Best for nociceptive pain

• Lemniscal system
  • Vc (VPL, VPm) nucleus, medial lemniscus, IC
  • Paresthesia-producing stimulation
  • Best for neuropathic pain
In 1989, T.G. had an adenocarcinoma resected from the R cheek.

A sharp, stinging and shooting pain started in R V2

Morphine at 540mg/24h provided no significant relief

In 1992, LVPM electrode was implanted at 7L, 20P, and 2V to the AC

Complete pain suppression at 10Hz, 0.2ms PW, and 1.7V
EFFICACY OF DBS
(LEVY ET AL. 2010)

- Long-term successful pain relief in 50% (19-79%)
- VPL stim for neuropathic pain: 56% achieved long-term relief
- PVG stim for nociceptive pain: 23% achieved long-term relief
- Overall 50-60% DBS patients report at least moderate levels of pain relief and/or have continued stimulator use at one year follow-up
FUTURE OF DBS SURGERY

- OCD (NIMH)
  - completion date: September, 2015
- Depression (Emory)
  - completed, pending analysis
- Pain syndrome (Cleveland Clinic)
  - completion date: Fall, 2014
- Morbid Obesity (OSU)
  - completion date: Jan, 2015
- Epilepsy (Medtronic)
  - completion date: October, 2015
AREAS OF FUTURE DIRECTION

- Depression
- Obsessive Diseases
- Addiction
- Tourette syndrome
- Obesity
Case Series: Deep Brain Stimulation in Patients with FXTAS

Randi J Hagerman1,2, Jamie S Pak3, Melina Ortigas1, John Olichney1, Robert Frysinger4, Madeline Harrison1, Edmund Cornman1, Danuta Z. Loesch1, Richard G Bittar1, Richard Peppard2, Lin Zhang1 and Kiarash Shahlaie1"*Corresponding author: Lin Zhang, MD, PhD, Lawrence J. Ellison Ambulatory Care Center, 4560 Y St, Suite 0100, Sacramento, CA, USA, 95817, Tel: (916) 734-7588; E-mail: lin.zhang@ucdmc.ucdavis.edu