Deep Brain Stimulation and Movement Disorders

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OBJECTIVES

• Understand the role of Deep Brain Stimulation (DBS) in movement disorders

• Understand the rationale for patient selection, benefits as well as risks of DBS in movement disorders
• 46 AD: Application of electric ray (torpedo torpedo) to cranium to cure headaches

• 19th century: Aldini stimulated exposed cortex and evoked motor response (grimacing prisoner)
  - 1880s: topography studies by surgeon Horsley

• 1950s: eloquent mapping of sensory and motor cortices by Penfield and colleagues

• 1938: Electroshock by Cerletti for psychosis

• 1950s Electrical stim for pain, functional stim for behavioral disorders
• 1947 Spiegel and Wycis fashioned the first human sterotactic frame

• 1949 Leksell fashions an arc-quadrant frame which still continues to be used

• Early stimulation studies (1950s-60s)
  - Delgado for seizures and psychosis
  - Bektherva for hyperkinetic movement disorders
  - Sem-Jacobsen for epilepsy and schizophrenia
  - Cooper for epilepsy, cerebral palsy and spasticity

• Micro electrode recordings Abel-Fessard 1961

• 1967: Introduction of levodopa, political pressures—functional neurosurgery briefly takes a back seat

http://www.neurosurgery.org/cybermuseum/sterootactichall/stereoarticle.html
• 1991 Benabid, Blond and Siegfried report effects of thalamic DBS on tremor

• 1990s Laitinen DBS to Gpi for parkinsons

• 1994 Pollack and colleagues demonstrated effects on STN DBS in Parkinsons

• FDA APPROVAL
  • 1997 ET
  • 2002 for PD (STN and GPi)
  • 2003 Humanitarian device exemption for dystonia (generalized and segmental)
  • 2009 HDE for OCD (ant limb IC)
NEUROSTIMULATION
MODULATION OF THE NERVOUS SYSTEM USING IMPLANTED/EXTERNAL DEVICES

TRANSCRANIAL MAGNETIC STIMULATION
http://etkinlab.stanford.edu/images/rTMScoil.jpg

CORTICAL STIMULATION
http://www.medgadget.com/2008/01/brain_stimulation_device_for_stroke_victims_fails_clinical_trial.html

DEEP BRAIN STIMULATION
CONDITIONS DBS IS USED FOR

FDA approved for Parkinson’s & Essential tremor

Humanitarian device exemption (HDE) for Generalized/segmental dystonia (genetic) and for OCD
MOTOR SYMPTOMS OF PARKINSONS

- Rigidity
- Tremor
- Bradykinesia
- Gait disorder
MOVEMENT DISORDERS AND THEIR IMPACT

PARKINSONS
- 1 MILLION people are currently diagnosed with PD in the United States
- 1 in 100 Americans over the age of 60
- 1.6% of Medicare beneficiaries

ESSENTIAL TREMOR:
- Most common movement disorder
- 0.4 to 3.9 % of the population, incidence maybe higher (Severe enough to warrant diagnosis)
- QUEST Scores higher than in PD
- DYSTONIA: limited data due to multiple forms
BASAL GANGLIA STRUCTURE

- Cortex
- Caudate nucleus
- Thalamus
- Globus pallidus
- Hypothalamus
- Substantia nigra
- Putamen
- Subthalamic nucleus
DBS - WHAT IS THE TARGET?

- ANTERIOR LIMB INTERNAL CAPSULE - OCD
- THALAMUS - TREMOR
- GLOBUS PALLIDUS INTERNA - PARKINSONS/ DYSTONIA
- SUBTHALAMIC NUCLEUS - PARKINSONS
- HYPOTHALAMUS - CLUSTER HEADACHE
STN vs. GPI

LANCET 2013

Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced Parkinson's disease: a randomized controlled trial.

INTERPRETATION:

Although there was no difference in the primary outcomes, findings suggest that STN could be the preferred target for DBS in patients with advanced Parkinson's disease.
HOW DOES DBS WORK?

• Short answer------- We don’t know!!

• Long answer
  • Initially thought to be similar to lesioning, inhibits electrical activity
  • Data suggests differential effects based on stim rate and location
    • High frequency stim works, frequencies lower than 50 Hz doesn’t
  • Axon stimulation (excitatory-capsule) vs neuronal stim (inhibitory)
  • ? Modulation more than inhibition
WHY SHOULD YOU CONSIDER DBS

• PARKINSONS (PD):
  • Tremor inadequately controlled by medications
  • DBS with significant advantage over best medical therapy for motor fluctuations
    On state without dyskinesias ~ 4hrs
    Off state decreased by ~ 2-4 hrs
    Improved PDQ 39 ~ 25%
    Benefits sustained upto 10 yrs

• ESSENTIAL TREMOR:
  • better than standard meds, improves ADLs, functional impact (60% or more improvement in tremor scores)

• GENERALISED DYSTONIA (HDE) (limited data):
  • DYT-1 responds really well, role of meds in generalized dystonia again limited
PATIENT SELECTION

• PARKINSONS:
  • PD and not Parkinson plus / drug induced parkinsonism
  • Ideally with motor fluctuations and maximum medical therapy, though emerging data for early implantation (EARLY STIM)
  • Not demented, screen mood disorders
  • Comorbidities (cardiac/ vascular/ coagulation disorders)

• ESSENTIAL TREMOR:
  • Tremor affecting quality of life/ function (moderate to severe tremor)
  • Ideally should have tried first line meds (beta blockers/ primidone)
  • Not demented

• DYSTONIA:
  • Case by case, through IRB, ideally generalized/ genetic torsion dystonia

OTHER INFLUENCING FACTORS: age, poor levodopa response in PD, family/ social support
EARLY STEROTACTIC SURGERY
DBS PROCEDURE

Stage I – Implant electrode
- Frame placement
- CT with frame
- CT/MR fusion & targeting
- Micro-electrode recording
- Macro Stimulation
- Implantation

Stage II
- Pulse Generator Placement
CURRENT DBS SURGERY OPTIONS

• **AWAKE:**
  – Frame bases
  – With MER
  – Frameless
  – With MER

• **ASLEEP:**
  – Frameless
  – MRI Guided
  – CT Guided
Role for Micro-Electrode Recordings

- Target localization is a combination of anatomic and physiologic localization
  - Anatomic (MRI-CT fusion and coordinates)
  - Physiologic (confirms intended anatomic target)

- MER (microelectrode recording)
  - Allows for confirmation of intended functional target (Vim thalamus, dorsolateral STN, Gpi)
  - Allows intra operative revision of intended sterotactic plan
DBS TRAJECTORY

Microelectrode pathway

Atlas of the basal ganglia

STN

Thalamic nuclei

Zona Incerta

SNr

Caudate

Neuronal recordings

MICROELECTRODE RECORDINGS
STIMULATION THROUGH THE LEADS:

- Goal to map out effects (improve tremor, rigidity)

- Map side effects (capsule, medial lemniscus, 3rd nerve fascicles)

- In some cases, mainly useful to map side effects (such as Dystonia)
Four variables

- Active contact in electrode (0,1,2,3-mono, bipolar/ double negative and so on)
- Amplitude of charge (in volts)
- Frequency (in hertz)
- Pulse width (in microseconds)

Contributes to infinite combinations but we start with tried and tested ones

- Low frequency (dystonia)
- High and mid range frequencies (PD and tremor)
- Higher pulse width (dystonia/ sometimes tremor)

Programming can take 3-6 mo or longer
Deuschl, NEJM Aug. 2006
- Randomized trial of DBS for PD
- 156 patients
- DBS + Rx vs. Rx alone
- End points: 6 mo PDQ-39 & UPDRS-III

**Outcomes favored DBS**

- **PDQ** 75% vs. 25% *(p<0.001)*
- **UPDRS** 85% vs. 13% *(p<0.001)*
OUTCOMES

Deuschl 2006
Goodman, et al 2006
100 Consecutive patients / 191 implanted devices

- **Infections** 7 (3.7%)
  - Cerebral infarct 1
  - Intracerebral hemorrhage 1
  - Subdural hemorrhage 1
  - Air embolism 1
  - Wound hematomas 2
  - Skin erosions 2
- Seizures 3
- Electrode revisions 6 (3.1%)
- Mortality 0
- Permanent deficits 0
- **TOTAL** 24 (13%)
ANNUALIZED VM COMPLICATION RATE

2007-2015

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### Table 4. Adverse Events during the Six-Month Study.

<table>
<thead>
<tr>
<th>Event</th>
<th>Neurostimulation Group</th>
<th>Medication Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Perioperative cerebral hematoma</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Suicide 5 mo after surgery</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Car accident during psychotic episode</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Readmission to the hospital</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Worsening of mobility</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Infection at the stimulator site</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Erroneous stimulator shut-off</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Vertebral fracture from fall</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hip fracture from fall</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total nonserious adverse events</td>
<td>77</td>
<td>96</td>
</tr>
<tr>
<td>Mild</td>
<td>35</td>
<td>8</td>
</tr>
<tr>
<td>Moderate</td>
<td>32</td>
<td>39</td>
</tr>
<tr>
<td>Severe</td>
<td>10</td>
<td>49</td>
</tr>
</tbody>
</table>

Deuschl 2006
LIMITATIONS OF SURGERY

• Improvement limited by patient’s best condition “on” medications

• Little effect on autonomic dysfunction

• Little effect on depression

• Akinesia, speech, postural stability, freezing of gait, and cognitive function worsen within 1 to 5 years

• Unknown (likely no) alteration in natural history of Parkinson’s Disease
OTHER RISKS

JAMEY VERSION 1.0
(2006 MODEL)

JAMEY VERSION 2.0
(POST DBS STN INSTALLATION)

HEAD BUMPAGE (2)
(HELPS KEEP HATS IN PLACE)

BIONIC IMPLANT
(DBS, GPS, MP3?)

UP-SIZED
BOILER ROOM
(+/- 30 LBS)

UPGRADED PANTS
WITH ‘SKOSH’ MORE ROOM TO ACCOMODATE NEW BOILER

“OLD MAN” STICK FOR POKING STUFF (AND WALKING)
THINGS TO REMEMBER

• DBS systems now (fully implanted Medtronic Activa system) are WHOLE BODY MRI COMPATIBLE

• Microwave, shortwave and ultrasound diathermy contraindicated

• Can be used in conjunction with pacemakers, as long as devices are compatible

• Newer devices not affected by household electronic equipment
FUTURE OF DBS

DEVICE RELATED:
- Battery life
- Remote monitoring
- Constant current
- Responsive neurostimulators
- Remote monitoring

EXPANDING THE HORIZON:
- Early PD
- Tourettes
- Cluster headaches
- Memory
- Epilepsy
- OCD

PROCEDURE RELATED:
- Awake vs asleep
- Miniature pulse generators
- CSF Glucose as power supply