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University of Colorado Anschutz Medical Campus
Director, OCD Clinic and Co-Director Neuromodulation Program
Medical Director, Student and Resident Mental Health

Conflicts of Interest
Ad Hoc Consulting for Medtronic

LEARNING OBJECTIVES
At the end of this presentation, participants should be able to:
• Summarize patient selection criteria for deep brain stimulation of the ventral capsular/ventral striatum under the FDA humanitarian device exemption
• Describe the anticipated response rate of deep brain stimulation of the VVC/V5 for OCD
• Identify the parameters that may be changed during DBS programming
What is DBS?

- Titretable
- Can be turned off
- Minimally invasive
- Mechanism Unknown
- Modifying Circuits

OCD - Ablative Surgeries

- Success rates of 50-60%
- Performed as early as the 1940’s


Anterior Limb of the Internal Capsule (ALIC)
(Ventral Capsule/Ventral Striatum, Nucleus Accumbens)

(Figure 8: Anatomy of the brain, courtesy of John Thompson, PhD)
1. What are the Guidelines for DBS for OCD (see previous email attachment)

Nuttin et al., 2014

Journal of Neurology, Neurosurgery and Psychiatry

Criteria for candidacy:
- Minimal clinical symptoms of OCD
- Disability and treatment-refractoriness
- Independent evaluation by expert in management of psychiatric disorder
- Suicidality
- Neuropsychological assessment – cognitive, psychiatric, interpersonal functioning, expectations for surgery

MULTI-DISCIPLINARY TEAM AT UCHealth

Pamela David-Gerecht, PhD
Research Coordinator

Michael Greher, PhD
Neuropsychology

Judith Gault, PhD
Research Assistant

Brian Hoyt, PhD
Neuropsychology

Rachel Davis, MD
Psychiatry

Drew Kern, MD
Neurology

Aviva Abosch, MD, PhD
Neurosurgery

Steven Ojemann, MD
Neurosurgery

Lisa Humes, PA
Neurosurgery

(Slide courtesy of John Thompson, PhD)
Rituals or routines
Distressing thoughts, fears or images
Obsessions

Compulsions
Rituals or routines

Life-time prevalence 1-3%

Treatment-Resistant Incidence:
- 40-60% OCD patients are refractory to conventional therapies, approximately 10% remain severely affected
- Potential candidacy for neurosurgical intervention

DEEP BRAIN STIMULATION FOR OCD
HUMANITARIAN DEVICE EXEMPTION – ALIC (VC/V5)

- Age greater than 18 and OCD diagnosis for at least 5 years
- Marked functional impairment
- YBOCS >/= 28 (severe – extreme OCD)
- Three 12 wk trials of serotonergic agents including clomipramine
- Augmentation with antipsychotic and long-acting benzodiazepine
- At least 20 sessions of ERP

EXCLUSION CRITERIA
- Bipolar disorder
- Psychotic disorder
- Active substance use disorder (within the past year)
- Severe personality disorder
- Active suicidality or self-harm behaviors
Evidence for efficacy of VC/VS DBS for OCD

Figure 1: Average (x±s.e.) change in depression (left) and anxiety (right) measures over time.

Greenberg et al., 2010, Mol Psychiatry.

Evidence for efficacy of VC/VS DBS for OCD

Figure 2: Average (x±s.e.) change in depression (left) and anxiety (right) measures over time.

Greenberg et al., 2010, Mol Psychiatry.

Evidence for efficacy of VC/VS DBS for OCD

Figure 3: Average (x±s.e.) change in depression (left) and anxiety (right) measures over time.

Greenberg et al., 2010, Mol Psychiatry.
YBOCS $\geq 28$ (severe – extreme OCD)

What does 50% Reduction look like?
What does 50% Reduction look like?

<table>
<thead>
<tr>
<th>Area</th>
<th># of studies</th>
<th># of pts</th>
<th>Response</th>
<th>Mean YBOCS reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC/VS (Ventral capsule/Ventral striatum)</td>
<td>6</td>
<td>51</td>
<td>100%</td>
<td>29.2</td>
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<tr>
<td>ALIC (Anterior limb of internal capsule)</td>
<td>6</td>
<td>15</td>
<td>100%</td>
<td>0</td>
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<td>NAc (Nucleus Accumbens)</td>
<td>5</td>
<td>33</td>
<td>100%</td>
<td>38</td>
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<td>STN (Subthalamic nucleus)</td>
<td>4</td>
<td>22</td>
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<td>31</td>
</tr>
<tr>
<td>STN + NAc</td>
<td>1</td>
<td>2</td>
<td>100%</td>
<td>71.2%</td>
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<tr>
<td>ITP (Inferior thalamic peduncle)</td>
<td>1</td>
<td>5</td>
<td>100%</td>
<td>51%</td>
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<tr>
<td>Combined</td>
<td>58.2%</td>
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DBS for OCD: Systematic Review and Evidenced-Based Guideline

Hamani et al., 2014, Neurosurgery, Involved - ASSFN, CNS, AANS

- Level I evidence: bilateral STN DBS
- Level II evidence: bilateral NAc DBS
- Insufficient evidence for unilateral DBS

DBS for OCD – Literature Review

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*Van Westen 2015, Curr Behav Neurosci Rep
Adverse Effects of DBS – VC/VS

<table>
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<th>Procedure Related</th>
<th>Superficial wound infection – 3.8% (N=1)</th>
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<tr>
<td></td>
<td>Seizures – 3.8% (N=1)</td>
</tr>
<tr>
<td></td>
<td>Intracerebral hemorrhages – 7.7% (N=2)</td>
</tr>
<tr>
<td></td>
<td>3.8% symptomatic – apathy, resolved in 3 mos</td>
</tr>
<tr>
<td>Device Related</td>
<td>Breaks in leads or extension wires – 7.7% (N=2)</td>
</tr>
<tr>
<td>Stimulation Related (Transient)</td>
<td>Increased suicidal ideation – 11.5% (N=4)</td>
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<tr>
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<td>Increased OCD severity – 11.5% (N=4)</td>
</tr>
<tr>
<td></td>
<td>Hypomania – 3.8% (N=2)</td>
</tr>
<tr>
<td></td>
<td>Irritability – 3.8% (N=1)</td>
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No statistically significant effects on neuropsychological testing

1Greenberg et al., Mol Psychiatry, 2010
2Goodman et al., Biol Psychiatry

Risks of DBS

Mental Status Δ: 9–18%
Infection/erosion: 2–11%
ICH: 0.6–13.3% symptomatic
Seizures: 0.9–9.1%
Lead migration: up to 8%
Hardware frx/Open circuit: 4.3–8.4%/electr yr
Environmental: rare
Stimulation "Failure": ?
*No standardized reporting of AE’s

Predictors of Response to DBS

More likely to respond
- Older age of OCD onset
- Symptom domain: sexual/religious
- Intraoperative laughter

Not a predictor of response
- Striatum vs. STN
- Gender
- Current age
- OCD duration
- Symptom domains: aggressive/checking, contamination/cleaning, symmetry/ordering, hoarding, somatic

Intraoperative laughter

1Wimo et al., PLOS One
2Yag et al., NeuroImage
Neurocircuitry
Cortico-striatal-thalamic-cortico (CSTC) pathways

Solid lines = glutamate (excitatory)
Dotted lines = GABA (inhibitory)


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Dotted lines = GABA (inhibitory)

Mechanism of DBS in OCD: involvement of cortico-striato-thalamo-cortical (CSTC) pathway

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<th>Target</th>
<th>Normal Function</th>
<th>Effect of DBS</th>
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<td>NAc</td>
<td>Reward processing (DA, 5-HT)</td>
<td>Normalizes NAc activity during reward processing;↑ 5-HT &amp; DA; Improve sensorimotor gating</td>
</tr>
<tr>
<td>STN</td>
<td>Excitatory glutamate</td>
<td>Normalizes hyperconnectivity between striatum and OFC;↑ decisional impulsivity and evidence accumulation</td>
</tr>
</tbody>
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Asleep Imaging-Based DBS Surgery

- No physiological confirmation

(Slide courtesy of Aviva Abosch, MD, PhD)
DBS PROGRAMMING PARAMETERS

- Amplitude (V): electromotive force
- Pulse Width (µs): the time of each cycle
- Frequency (Hz): the number of cycles per unit time
- Which contacts to stimulate through (0, 1, 2, or 3)
- Electrode Configuration: monopolar vs. bipolar

F (Hz) = velocity/wavelength

- 2-10 V
- 90-150 Hz
- 60-210 µs

References


References


