Brain Stimulation in Psychiatry

Marc Heiser MD PhD
LAC DMH Clinical TMS Program
Assistant Clinical Professor
Department of Psychiatry and Biobehavioral Sciences
UCLA David Geffen School of Medicine
Disclosures

• None
How Do We Change Brain Activity?

- Neuromodulation
  - tDCS
  - DBS
  - TMS
  - TNS
- Medications
- Environment
- Therapy
- Brain Training
Learning Goals

• Define transcranial magnetic stimulation (TMS) and how it works
• Become familiar with the concept of neuromodulation and how TMS fits within it
• Know which clients may benefit from TMS
• Be able to educate clients about TMS basics
Definitions: TMS

• Transcranial – across the skull
• Magnetic – uses magnetic fields
• Stimulation – activation of neurons or nerves
How Does A Magnet Stimulate Neurons?

• Faraday’s Law of electromagnetic induction (1831)!
  – A changing magnetic field produces electric current in a wire
  – Neurons are wires
We Can Produce Magnetic Fields With Electricity

- Run large, brief current through wire, and create strong magnetic field

Electric current in wire → Magnetic field → Electric current in brain → Activate neurons!
How do MRI and TMS Differ?

<table>
<thead>
<tr>
<th></th>
<th>MRI</th>
<th>TMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnetic Field Strength</td>
<td>1.5 Tesla</td>
<td>2 Tesla</td>
</tr>
<tr>
<td>Rate of Change of Magnetic Field</td>
<td>20 T/s</td>
<td>20,000 T/s</td>
</tr>
<tr>
<td>Induces Current in Brain</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Effect of TMS is Focal

- Depends on coil configuration
- Stimulate 1cm³ volume
- Depth of ~2cm
TMS Is Old!

Thompson SP. 1910

Barker, Jalinous, & Freeston, 1985
TMS Can Change Brain Activity

• The pattern of pulses determines the effect of TMS on brain area – “dose”
  – Low frequency pulses inhibit brain activity
  – High frequency pulses enhance

[Diagram of different patterns of pulses for LF rTMS, HF rTMS, cTBS, and iTBS]
Other TMS Variables

• Where – location of coil

• How strong – intensity of magnetic pulses

• How many – number of pulses

• Repeated stimulation produces lasting effects
  – “Neurons that fire together wire together”
Brain Activity Is Altered In Depression

- Altered cortical activity in depressed patients
- Hypofunctioning of DLPFC
- Enhance activation using rTMS

A PET scan measures vital functions such as blood flow, oxygen use and blood sugar (glucose) metabolism.

Source: Mark George, M.D. Biological Psychiatry Branch Division of Intramural Research Programs, NIMH 1993
Neuronetics TMS Trials

- Double-blind randomized controlled trials
- Control is a Sham TMS coil compared to Active TMS
- Antidepressant free
- 20-30 treatments
TMS for Adult Depression

• Oreardon et al. n = 301 adults
• Significant difference in proportion of response and remission rates favoring active vs. sham

Study 101: Significant Clinical Effects on MADRS Categorical Measures

Oreardon et al. Biological Psychiatry, 2007
TMS for Depression

• FDA approved since 2008 for patients with depression who have failed at least 1 antidepressant

• 3 large RCT – two industry sponsored, one NIH, numerous smaller trials showed reduction in depressive symptoms compared to sham treatment

• More recent meta-analyses show about 30-50% response and 20-30% remit (placebo 10, 5%), NNT 6 and 8 (Berlim 2014)

O’Reardon Biol Psychiatry 2007; George Arch Gen Psychiatry 2010; Levkovitz World Psychiatry 2015
Effects are Durable and Meaningful

- Durability – at 12 months 62% of initial responders remained, 36% had more TMS (Dunner 2013)

- Improvement in quality of life and functional status acutely and at 6 months (Solvason 2014)
TMS is Safe with Minimal Side Effects

• Local discomfort and headaches – decreases over course of treatment (Brockhardt 2013)

• Seizure risk – 1:50000 treatments (same as medication)
Compared to Medications

DRUG THERAPY vs. TMS THERAPY

- Insomnia
- Dry Mouth
- Blurred Vision
- Fatigue
- Nausea
- GI Distress
- Weight Gain
- Sexual Dysfunction
- Scalp Discomfort
TMS Is Standard Treatment in Psychiatry, Not Experimental

• American Psychiatric Association: Best practice guidelines for treatment of depression

• Department of Veterans Affairs: National evidenced-based rTMS rollout for treatment of depression

• TMS for depression is now covered by most private insurance and Medicare

• Cost-effective after first medication failure (Voigt et al PLOS One 2017)

• Not offered by public mental health providers
Significant difference in response rate by duration of treatment ($p<0.01$)
Significant difference in response rate by intensity of stimulation ($p<0.05$)
Significant difference in response rate by number of pulses per day ($p<0.05$)
Optimizing Treatments

• New protocols
  • Left vs. Right sided treatment
  • Bilateral treatment
  • Theta burst
    • 10Hz standard (37min) vs Theta burst (3min)
    • N = 414
    • Outcomes same between groups
      • Response = 47% 10Hz vs 49% TBS; Remission 27% vs 32%

Blumberger et al NEJM 2018
Other Uses

• Geriatric depression
• Bipolar depression (Nahas 2003)
• Suicidal crisis (George 2014)
• Schizophrenia (Slotema 2014)
• OCD (Berlim 2013)
• Substance use disorders (Enokibara 2016)
• PTSD (Karsen 2014)
• Autism
• Cognitive impairment/Traumatic brain injury
• Pain
• Eating disorders
Who Should Not Get TMS? Contraindications

• Metal implants in skull
  – Cochlear implants
  – Ferromagnetic vascular clips
  – Shrapnel
• Seizure disorder
• Clients may continue medications
  – Monitor for meds linked to seizures
  – Changes in medications – especially benzodiazepines, anticonvulsants
• Risk of inducing mania
What Is It Like To Get TMS?

- Sessions 5d/week x 4-8 weeks
- Sitting in chair, awake
- Sensation: Hearing clicking, feel tapping on scalp
- Treatment lasts about 3-35 minutes
- Can be paused or stopped at any time
- When done, may return to normal activity
## TMS Vs. ECT

<table>
<thead>
<tr>
<th>TMS</th>
<th>Electroconvulsive Therapy (ECT)</th>
</tr>
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<tbody>
<tr>
<td>Focal targeting with Magnetic Field</td>
<td>Electric current flow is diffuse</td>
</tr>
<tr>
<td>Awake and Alert</td>
<td>Under brief anesthesia</td>
</tr>
<tr>
<td>No seizure intended</td>
<td>Seizure (convulsion) induced</td>
</tr>
<tr>
<td>No change in vital signs</td>
<td>Significant incr in heart rate and BP</td>
</tr>
<tr>
<td>No impairment of cognition</td>
<td>Amnesia and other cognitive effects are common</td>
</tr>
<tr>
<td>Course of treatment: 20-30 sessions</td>
<td>8-16 treatments more typical</td>
</tr>
<tr>
<td>Can be given while taking meds (off-label but common practice)</td>
<td>Many centers require wash-out of medications before treatment</td>
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LAC DMH TMS Program

LAC DMH: 40,000 People Treated for Depression (2016-17)

~20,000 With Refractory Symptoms

How can we help these individuals?
MHSA Innovations Funding

• 3 year pilot project
• Obtain TMS device and fund support staff
• Treat clients in LAC DMH outpatient clinics
• Report on outcomes
• Expand if appropriate
Client Criteria for TMS Program

- Major depressive disorder or other disorder w/depression (SAD, dysthymia, Bipolar depression)
- Inadequate response to at least one antidepressant
- No seizure disorder
- No metal implants in head (dental ok)
- Likely to adhere to treatment (attend 5 days/week)
- Not conserved
LAC DMH TMS Process

- Referral form in EMR can be completed by clinicians and/or psychiatrist (would want current treating psychiatrist to be aware)
- TMS psychiatrist will perform evaluation and assess appropriateness for TMS, explain procedures and obtain consent
- TMS psychiatrist or other team members will perform TMS treatments with ongoing consultation with primary treatment team
- Client will continue to see primary providers as scheduled
- Client may continue medications during TMS treatment course
- Outcomes are measured every week – HAMD, QIDS, PHQ9
- Final client survey
LAC DMH TMS: Progress Thus Far

• Began June 2019
• 27 referrals
• 23 evaluated
• 18 treated/in-treatment
• 10 completed treatment
• 1 drop out due to intolerance, 1 due to substance relapse
• 6 now in treatment
LAC DMH TMS: Client Responses

- Clients are adherent
- Several remissions
- Responses are positive: “In the last 7 years she had suffered many episodes of anxiety and depression. She took many medications with minimum impact on her wellbeing. Now she has shown great improvements. For instance, she smiles more, is more likely to go on walks, has more energy…”
The Future of TMS

• New indications
• Peds/adolescent psych
• Neuronavigation
• Personalized TMS: Guided by symptoms, fMRI, EEG
• Take-home devices
A Revolution: Other Neuromodulation Techniques

- Goal is to provide more specific treatments based on understanding of neurophysiology/anatomy
Trigeminal Nerve Stimulation (TNS)

- Initially used for seizure disorders
- 2019 - FDA approved for children w/ADHD
  - Double blind placebo RCT
  - 62 children, 8-12 yo
  - 4 weeks, nightly tx
  - Reduction in ADHD-RS score, improved CGI, NNT 3
  - Comparable to non-stimulant medications
  - Ongoing studies for insomnia, autism

McGough et al. JAACAP 2019
Transcranial Direct Current Stimulation (tDCS)

- Can be used to make the brain more or less excitable
- In home use, very simple technology
- Being marketed for everything, but also used in academic research
Invasive Neuromodulation

Deep Brain Stimulation (DBS)

Breakthrough device translates brain activity into speech

By Nicholas Weiler, UCSF
Thursday, April 25, 2019

Neuralink
Conclusions

• Neuromodulation is advancing rapidly along with our understanding of the brain basis of psychiatric symptoms
• TMS is safe and effective for treatment of depression and likely other psychiatric symptoms
• TNS is a new, safe, effective treatment for ADHD
• Be on the lookout for more!
Questions

• Mheiser@dmh.lacounty.gov
Outline

• What is TMS
  – Definition
  – How it works
    • Physics
    • Parameters
    • Neuroscience

• Clinical uses of TMS
  – Depression
    • Evidence for efficacy
    • Treatment protocols
  – Other uses
  – Compare to ECT

• Devices
  – rTMS
  – Deep TMS

• Patient experience

• Our program

• Future of TMS
  – Neuronavigation
  – Brain imaging for targets
  – Symptom specificity
  – EEG – Neosync

• Other neuromodulation techniques
  – TNS for ADHD
  – DBS
  – tDCS
Conclusions

• TMS is a safe, effective treatment for depression and may be beneficial for other psychiatric disorders

• Many patients in LAC DMH have depression among other symptoms and may benefit from TMS

• Mobile TMS will bring this treatment directly to these patients and into public mental health!
Questions and Feedback