Advances in Neuromodulation for Psychiatric Practice

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Chief Medical Information Officer

Brent G. Nelson, MD wears multiple hats...

PrairieCare

11 locations
180,000 visits per year
All payors including Medicare and Medicaid

71 bed inpatient - child /adol
Residential – child /adol
PHP - child /adol
IOP - all ages
Clinic - all ages
TMS - adult
Disclosures

- I will be talking about prescription medications and FDA approved neuromodulation procedures and devices.
- I will be talking about off label use of medications and procedures.
- I do not have any financial interests in any neuromodulation companies or products discussed today.
- I do serve on the scientific advisory board of RefactorHealth, a digital diagnostics company based in New Haven, CT.

Objectives

1. Describe the historical development, physics, and function of non-surgical neurostimulation.
2. Understand the efficacy provided by different neurostimulation devices.
3. Identify clinical history and diagnoses required for treatment with each device.

Mental Health Landscape

- 1.5 billion people worldwide
- 64 million Americans
- 1.1 million Minnesotans
Depressive Disorders

- 400 million people worldwide, 14.8 million adult Americans
- $210.5 billion in annual direct and indirect costs with $12 billion alone in lost workdays each year
- Leading cause of disability in US (ages 15-44) and worldwide (WHO)
- Suicide is the second leading cause of death among 15 - 29 year olds
- Co-occurs with many other conditions
  - Type 2 Diabetes
  - Multiple Sclerosis
  - Epilepsy

Nicotine Dependence

- One fourth of the population uses tobacco products and 10.4 percent smoke cigarettes
- 17.7 million – smoking-related deaths (between 1964 and 2012)
- 480,000 – deaths annually
- 5.6 million – Americans currently younger than 12 will die prematurely from smoking-related disease
- $200 billion – the annual societal costs due to smoking in the US
- $150 billion – direct medical care of adults
- $150 billion – lost productivity due to premature deaths
- $5.6 billion – lost productivity due to exposure to secondhand smoke
- 70 percent of current smokers’ excess medical care costs could be prevented by quitting

Obsessive Compulsive Disorder

- Lifetime and 12 month prevalence estimates are 2.3% (1.9) and 1.2% (1.0)
- 28.2% of respondents reported experiencing obsessions or compulsions (O/C) at some time in their lives
- Most of these respondents experienced only one of the nine O/C types most commonly checked (15.8%), hoarding (14.9%), ordering (14.9%), or washing (9.6%)
- The male age of onset of OCD is 19.5 years
  - Males: majority of very early onset cases, with 25% of males having onset before age 10
  - Females: mean age of onset of 10.9 years, with the highest slope during adolescence
  - There are fewer new cases among males and females after the early 30s
  - Those who develop OCD spend a mean of 6.4 years of life (SE = 1.1) with the disorder
  - Two thirds (65.3%) of 12-month cases reporting severe impairment
  - Treatment rates were much higher for cases rated severe (92.4%) than moderate (60.4%) on the Y-BOCS, although only a minority of severe cases (36.4%) or moderate (13.8%) cases received treatment specifically for OCD.

Neuromodulation

The term “neuromodulation” encompasses a broad array of treatments, both electrical and chemical, targeting a variety of locations in the body to best achieve the desired outcome.

- International Neuromodulation Society

Neuromodulation Types

- Psychopharmacology
- Psychotherapy
- Brain Stimulation
- Exercise
- Acupuncture
- Yoga
- Massage
- Nutrition

Many others...
Nomenclature

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Vagus Nerve Stimulation

59 patients
Response: 30.5% (HRSD28), 33.9% (MADRAS), 37.3% (CGI-I)
Remission: 15.3% (HRSD28)


Deep Brain Stimulation


Closed Loop Devices

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Low Energy

High Energy

Conduction

Georg Simon Ohm (16 March 1789 – 6 July 1854) was a German physicist and mathematician.
Induction

\[ \nabla \times \mathbf{E} = \frac{dB}{dt} \]

Michael Faraday (1831) - Qualitative

James Clerk Maxwell (1860s) - Maxwell-Faraday Equation

"Faraday emf experiment" by Eviatar Bach

Silvanus P. Thompson (1910)

Jacques-Arsène d'Arsonval (1896-1940)

Induction in Action

Golestanirad et al., 2012
“Modern” Developments

1959 - Kolin et al. use magnetic fields to induce muscle contractions in frogs.

1965 - Bickford and Femming non-invasively stimulate human peripheral nerves via pulsed magnetic field.


1982 - Polson et al. use EMG to record magnetically induced motor jerks.

1985 - Anthony Barker in England with the “Sheffield Magnet.”

Progress

1988 - Shoogo Ueno develops figure 8 coil.

1991 - Pascual-Leone et al. report first speech arrest via rTMS.

MDD Circular and Figure 8

1995 - Kolbinger et al. undertake first proof-of-principle study with depression using flat, circular coil.

1996 - First meeting of TMS safety consensus group.

1998 - Wasserman publishes first TMS risk and safety guidelines.
### Motor Threshold Mapping

- TMS Single Pulse
- Motor Evoked Potential

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### Repetitive TMS (rTMS)

- 1 Train
- Multiple Stimuli
- Intertrain Interval

- High Frequency (>10Hz) Train: Stimulatory
- Low Frequency (<10Hz) Train: Inhibitory

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### MDD Figure 8 Modified

- 2007 - O'Reardon et al publish depression study utilizing Neurostar system
- 2008 - FDA approves Neurostar device for MDD
- 2010 - NIMH Trial (OPT-TMS) is completed
Neuronetics Trial (N=301)

A. MICRO-Reponse Rate (100% Improvement/Baseline)

100% MT, 10 Hz frequency, train duration of 4 s, inter-train interval of 26 s, and 75 trains per session, leading to a total of 3000 pulses over 37.5 min.

B. MICRO-Response Rate (100% Improvement/Baseline)

C. MICRO-Response Rate (100% Improvement/Baseline)

Engineering Diversity

Substantially Equivalent
MDD H1 Coil

1996 - NIH begins development of H1 coil
2001 - NIH Patents H1 coil
2003 - Brainsway founded and licensed exclusively
2013 - Brainsway is FDA approved for MDD

Brainsway Trial

MDD Criteria For Treatment

Diagnoses:
296.23 Major depressive affective disorder single episode severe degree without psychotic behavior
296.33 Major depressive affective disorder recurrent episode severe degree without psychotic behavior

Criteria:
- Lack clinical response to 6 trials of pharmacological agents in the current episode. This means at least 3 different classes, at or above the minimum effective dose and duration. Make sure this includes at least 3 evidence-based augmentation therapies.
- Inability to tolerate 4 agents with distinct and documented side effects.
- A documented response to TMS in a previous episode.
- A documented response to ECT in a previous or current episode or inability to tolerate ECT and TMS is considered less invasive.

AND MUST HAVE THE FOLLOWING:
- A trial of an evidence-based psychotherapy with adequate frequency and duration with significant improvement in symptoms as documented by rating scales.
Candidate Screening

Warnings:
- Seizure disorder or any history of seizures (except those induced by ECT or isolated febrile seizures in infancy or childhood which have been treated) should be given particular consideration.

Exclusions:
- Psychosis
- Active suicidal ideation
- Neurologic conditions including memory impairment, cerebrovascular disease, dementia, increased intracranial pressure, severe head trauma, or CNS tumors
- Persons with conductive, ferromagnetic or other magnetic-sensitive metals implanted in their head which are not removable and within 30 cm of the TMS magnetic coil. Examples include: cochlear implants, implanted electrodes/stimulators, aneurysm clips or coils, and bullet fragments. Dental amalgam fillings are not considered acceptable for use with TMS.

Treatment Timeline

Step 1 Referral by Primary Psychiatrist
Step 2 Evaluation by TMS Psychiatrist
Step 3 Prior Authorization by Payer

Step 4 Monday Tuesday Wednesday Thursday Friday
Week 1 MTM + Tx Tx Tx Tx Tx
Week 2 MT + Tx Tx Tx Tx Tx
Week 3 MT + Tx Tx Tx Tx Tx
Week 4 MT + Tx Tx Tx Tx Tx

MTM - Motor Threshold Mapping (60 min appt)
MT - Motor Threshold Determination (45 min appt)
Tx - Treatment (30 min appt)

Deep rTMS (dTMS)

2 sec Train 36 Stimuli
20 sec Intertrain Interval
55 Total

20 Treatment Sessions
20 Minutes Per Session

Table of Parameters
- Session Intensity: 120% of Motor Threshold (MT)
- Preheating: 2 min
- Treatment train duration: 2 seconds
- Intertrain interval: 20 seconds
- Total Treatment Duration: 20.2 minutes
- No. of Treatments: 20
- Number of pulses administered per session: 1980

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Real World Results

- **CGI-S Outcomes**
  - Overall response: 37.8%
  - Low response: 24.9%
  - High response: 14.4%

- **IOS-SR Outcomes**
  - Percentage meeting criteria: 45.7%
  - Percentage maintained: 25.2%

Maintenance of Effect

- 257 pts, 120 / 257 met response/remission criteria
- 62.5% continued to meet response at one year

Dunner et al., 2014

Carpenter et al., 2012
61% of unmedicated treatment resistant depression patients who did not respond to acute TMS treatment responded after four weeks of twice weekly deep TMS in the Brainway pivotal trial.

Appelkamp C, Yip AT, Mark S, George A, Young Center, Above B, Abraham Z, Carpenter J.

Images courtesy of BrainsWay
OCD H7 Coil Results

Efficacy and Safety of Deep Transcranial Magnetic Stimulation for Obsessive-Compulsive Disorder: A Prospective Multicenter Randomized Double-Blind Placebo-Controlled Trial


OCD H7 Coil Results


H7 OCD and MDD Results

Why Does It Work?

Activity Dependent Plasticity

Thiri Burst

Connectivity Stimulation

Resting-state connectivity biomarkers define neurophysiological subtypes of depression


Thank you!