Transcranial Magnetic Stimulation: TMS

A proven non-drug treatment for depression

Presented by:
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& Ian Cox
TMS Center of Madison

- Opened in January of 2013
- Collaboration between Rosecrance and Connections Counseling

Understanding the Problem
Major Depression: A Large Patient Population Currently Being Underserved

- **16.1 Million** US Adults with MDD
- **7.2 Million** Treated
- **4.5 Million** Poorly Served

Lack of efficacy

Intolerable side effects


Top 10 Causes of Disability
A Major Burden for Society Today

1. Lower Respiratory Infections
2. Diarrheal
3. **Unipolar Major Depression**
4. Ischemic Heart Disease
5. HIV/AIDS
6. Cerebrovascular Disease
7. Premature Birth
8. Birth Trauma
9. Road Traffic Accidents
10. Neonatal Infections

Brain Activity is Reduced in Depression

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

Repeated Activation of Left Prefrontal Cortex is Known to Produce Antidepressant Effects

- Neuroimaging studies have documented changes in functional connectivity between tissue directly stimulated by NeuroStar TMS and in deep brain regions known to be involved in mood regulation

Figure reproduced with permission of MJ Dubin, MD, PhD, Weill Cornell Medical College
Theory of Neuroplasticity

Unstimulated  Stimulated

Treating the Brain as an Electrochemical Target

Brain activity can be altered through:

TMS: is focused, non-invasive & non-systemic

DRUG THERAPY: Action is anatomically diffuse and systemic
Best Practices Treatment Guideline for Depression
Based on 2010 APA guidelines and NeuroStar TMS Therapy® indication for use.

STAR*D Study
demonstrates that current treatment has limited effectiveness

Adapted from: Practice Guideline for the Treatment of Patients with Major Depressive Disorder, 3rd Edition, APA (2010)
Likelihood of discontinuing treatment increases with each new medication attempt

<table>
<thead>
<tr>
<th>Treatment Attempt</th>
<th>Discontinuation due to side effects (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-Line</td>
<td>8.6%</td>
</tr>
<tr>
<td>Effect n=2876</td>
<td></td>
</tr>
<tr>
<td>One Prior</td>
<td>23.1%</td>
</tr>
<tr>
<td>Treatment Failure n=727</td>
<td></td>
</tr>
<tr>
<td>Two Prior</td>
<td>35.2%</td>
</tr>
<tr>
<td>Treatment Failures n=221</td>
<td></td>
</tr>
<tr>
<td>Three Prior</td>
<td>41.4%</td>
</tr>
<tr>
<td>Treatment Failures n=58</td>
<td></td>
</tr>
</tbody>
</table>

Neuronetics, Inc. (data on file)

TMS Therapy Avoids the System Side Effects
Commonly Experienced with Antidepressant Medications

TMS Side Effects
- Scalp Pain or Discomfort at Treatment Site

Systemic Drug Side Effects
- Weight Gain
- Constipation
- Diarrhea
- Nausea
- Drowsiness
- Nervousness
- Anxiety
- Increased Appetite
- Decreased Appetite
- Decreased Sexual Interest
- Headache/Migraine
- Abnormal Erections
- Impotence
- Dry Mouth
- Fatigue
- Dizziness
- Tremor
- Sweating
- Treatment Discontinuation Side Effects

Adverse Events occurring at an incidence >5% and 2x the rate of placebo treatment

## Primary Differences: TMS vs ECT

<table>
<thead>
<tr>
<th>TMS</th>
<th>ECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Non-invasive</td>
<td>• Invasive</td>
</tr>
<tr>
<td>• Minimal Side Effects</td>
<td>• Significant Risk of Side Effects</td>
</tr>
<tr>
<td>• No Seizure</td>
<td>• Seizure Required</td>
</tr>
<tr>
<td>• Active participant during the session</td>
<td>• Anesthesia Required</td>
</tr>
<tr>
<td>• Brief Interruption in one’s day</td>
<td>• Cannot Drive afterwards</td>
</tr>
</tbody>
</table>

### NeuroStar TMS Therapy® System

- **Cleared in October 2008 by the FDA** for the treatment of patients with major depression.
- Utilizes a highly focused **MRI-strength magnet** to stimulate nerve cells in an area of the brain thought to control mood.
- Stimulating these neurons, causing the release of neurotransmitters and clinical effects.
TMS in Clinical Practice

- Non-invasive
- No anesthesia or sedation
- No systemic side effects
- No negative impact on cognition
- Tolerable treatment with less than 5% discontinuation rate
- 37 minute outpatient procedure easily performed in a physician’s office
- 6 week treatment course
- Antidepressant medications may still be used during TMS treatments

PATENTED IRON CORE COIL

**Precision Pulse TMS® Technology**
- Targeted stimulation of the prefrontal cortex that activates deeper brain regions
- Flexible product design allows for high volume clinical use across a broad range of depression patient profiles

**Releases neurotransmitters**
**Increases cerebral blood flow**
**Increases glucose metabolism**
Proven Safety and Tolerability Profile

- Non-systemic, avoids the side effects commonly associated with antidepressant medications
  - No adverse effect on cognition
  - No adverse effect on sleep
- Excellent treatment adherence with less than 5% discontinuation rate due to adverse events
- Post marketing experience confirms a rare risk of seizure with NeuroStar TMS (<0.1% per patient)

**MEDICATIONS:** Other adverse events are nervousness, weakness, abnormal ejaculation, constipation, anxiety, impotence, diarrhea, increased appetite, dizziness, sweating, decreased appetite, tremor, drowsiness, decreased sexual interest, headache/migraine, blurred vision, and treatment discontinuation side effects.

**NEUROSTAR:** Eye pain, toothache, muscle twitching, facial pain, pain of skin.


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**NeuroStar TMS Therapy® System**

**Precision Pulse TMS®**

- Patented Iron Core Coil: Efficiently transfers electrical energy into magnetic field for uninterrupted treatment.
- 3D Coil Positioning System: Provides targeted stimulation of the prefrontal cortex that achieves deeper brain regions.

**Gantry and Base:** Supports the Treatment Coil and allows accurate maintenance of position throughout treatment, reducing the burden on the system operator.

**Iron Core Coil:** Designed for therapeutic use in multiple clinical practice settings.

**Graphical User Interface:** Intuitive software guides system operator through step-by-step treatment workflow.

**MT Assist®:** Unique software makes finding the right treatment dose easy.

**Centralized Database:** Manages all NeuroStar patient data.

**Custom Reports:** Improves outcomes tracking.

**Web-enabled Technology:** Accesses data from multiple systems and locations.
"...the use of an electromagnet to treat severe depression deserves a term that researchers hate to use: breakthrough."
Top Behavioral Health Hospitals Provide TMS Therapy

- Johns Hopkins Hospital
- Mayo Clinic
- McLean Hospital, Belmont, Mass.
- New York-Presbyterian University Hospital of Columbia and Cornell
- UCLA Semel Institute for Neuroscience & Human Behavior
- McLean Hospital
- Sheppard and Enoch Pratt Hospital

Proven Efficacy Demonstrated Through Randomized Controlled Trials

In an NIMH-funded, independent, randomized controlled trial, patients treated with TMS using the NeuroStar TMS System were four times more likely to achieve remission compared to patients receiving sham treatment \( (P = 0.0173, \text{ odds ratio} = 4.05) \)

O’Reardon, et al. (2007) Biological Psychiatry; George, et al. (2010) Arch Gen Psychiatry
Consistent Response and Remission Rates Across a Broad Range of Treatment Resistance

1 in 2 Patients Respond, 1 in 3 Patients Achieve Remission

**CGI-S Outcomes in Acute Phase**

<table>
<thead>
<tr>
<th>% of Patients (N=307)</th>
<th>Overall (N=307 total)</th>
<th>Low Treatment Resistance* (N=140)</th>
<th>High Treatment Resistance** (N=167)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Response (CGI-S ≤3)</td>
<td>Remission (CGI-S ≤2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>58.0</td>
<td>37.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>69.4</td>
<td>39.9</td>
<td></td>
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<tr>
<td></td>
<td>66.8</td>
<td>34.9</td>
<td></td>
</tr>
</tbody>
</table>

Naturalistic, Open Label Treatment Utilization and Outcomes Study

Patient reported outcomes (PHQ-9) were consistent with physician rated outcomes

LOCF Analysis of intent-to-treat population

*N* ≤1 adequate antidepressant medications; **≥2 adequate antidepressant medications

Carpenter, et al. (2012), Depression and Anxiety

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NeuroStar is the Only TMS System with Proven Durability Measured Over 12 Months

68% of study population in response, 45% in remission

**CGI-S Outcomes Post Acute Phase**

<table>
<thead>
<tr>
<th>% of Patients (N=257)</th>
<th>End of Acute</th>
<th>3 Months</th>
<th>6 Months</th>
<th>9 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Response (CGI-S ≤3)</td>
<td>Remission (CGI-S ≤2)</td>
<td>Response (CGI-S ≤3)</td>
<td>Remission (CGI-S ≤2)</td>
<td>Response (CGI-S ≤3)</td>
</tr>
<tr>
<td></td>
<td>62.3</td>
<td>41.2</td>
<td>62.3</td>
<td>43.2</td>
<td>66.1</td>
</tr>
</tbody>
</table>

36.2% of patients received NeuroStar TMS reintroduction (avg. of 16 treatments)

Physician directed standard of care

Long term durability of effect has not been established in a randomized controlled trial

LOCF Analysis of intent-to-treat population

Neuronetics, Data on file, NCT 00104611
# Areas of Ongoing Research in Investigator-Initiated Studies

- **Depression**
  - Adult depression
  - Adolescent and teen depression
  - Depression during pregnancy
  - Postpartum depression
  - Breast Cancer Patients With Depression and Anxiety
  - Imaging Biomarkers for TMS Treatment of Depression
  - Assessing brain response to rTMS in depression patients using simultaneous functional Near Infrared Spectroscopy (fNIRS)
  - Predictive and response biomarkers of effective treatment with TMS for MDD

- **Pain**
  - Women with chronic widespread pain
  - Pain and depression in patients with fibromyalgia
  - Chronic neuropathic pain
  - Role of the supraspinal opioidergic circuit in prefrontal rTMS-induced analgesia

- **Tinnitus**
  - Tinnitus

- **Addiction**
  - Nicotine craving / smoking

- **Schizophrenia**
  - Auditory hallucinations in schizophrenia

- **Other**
  - Testing TMS safety in presence of surgical clips
  - Near Infrared Spectroscopy (NIRS) to Investigate rTMS

- **Anxiety**
  - Generalized anxiety disorder
  - fMRI-guided TMS for generalized anxiety disorder

- **PTSD**
  - TMS for suicidal ideation PTSD

Limited to investigational use in these areas. Investigators are responsible for ensuring clinical protocols have been reviewed by an Institutional Review Board and meet applicable regulatory requirements for investigational use.

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# TMS Therapy: Real World Outcomes
Case Study: Jack

Jack is a 60-year-old male referred by his psychiatrist. He has a history of depression that dates back to 1998. He was hospitalized in Fort Collins, Colorado. He has been on medication and in counseling since essentially that time. He is diagnosed with PTSD, Major Depression and possible Bipolar 2 Disorder. Jack suffered sexual abuse and verbal abuse at the hands of his parents and other family members when he was a child. He was initially diagnosed with Major Depression and started on Prozac. This did not work for him. He remembers trying Wellbutrin and Paxil. Wellbutrin was not effective and Paxil gave him serious side effect. Throughout the years he has also been on Effexor, Cymbalta and Seroquel, with minimal to no efficacy. He has been on lithium for the last 13 years and Lamictal for approximately ten years. He took Namenda for about three months several months ago but this was not effective either.

Jack: Progress over 6 weeks

“I’m not sure how many weeks it’s been [since I finished] maybe 4, but doing great. I wake up every day and stop and then say, I’m not depressed! I asked my wife if it’s a sin to feel this good. Thanks for giving my life back!!!” - Jack
Where Can I find Help?

More than 650 NeuroStar® Locations in the U.S.
Does Insurance Cover the Cost of TMS?

230M Covered Lives

Anthem BCBS
BCBS of Alabama
BCBS of Arizona
BCBS of Florida
BCBS of Kansas
BCBS of Kansas City
BCBS of Louisiana
BCBS of Massachusetts
BCBS of Michigan
BCBS of Minnesota
BCBS of Nebraska
BCBS of Northeastern PA (NEPA)
BCBS of Rhode Island
BCBS of South Carolina
BCBS of Tennessee
BCBS Vermont
Blue Care Network
Blue Cross of Idaho
Blue Shield of California
BMC HealthNet
Cahaba Medicare
CareFirst Blue Cross
CommunityCare of Oklahoma
EmblemHealth
 Fallon Community Health of Massachusetts
FEHP (Fed Blue)
First Coast Service Option
Harvard Pilgrim Health Care
Hawaii Medical Services Assoc
HCSC
Health Net
Health New England
Health New York
Health Plan of Nevada
Highmark BCBS
Horizon BCBS of New Jersey
Humana, Inc.
Independence Blue Cross
Kaiser Permanente Oregon
MHP Health Care
National Association of Letter Carriers
Neighborhood Health Plan of Rhode Island
Medicaid
NGS (Medicare)
Novitas Medicare JH
Novitas Medicare JL
Optima Behavioral Health
Optum/United Behavioral Health*
Palmetto GBA
Premiere Blue Cross
Priority Health
Rocky Mountain Health Plan*
Tufts Health Plan
UHC Community Plan (Medicaid of New England)
UniCare (Massachusetts State Employees)
Vermont Medicaid
WA State HCA

As of 7/1/15
Madison Area Insurance Providers

CPT® Category I Codes

Therapeutic repetitive transcranial magnetic stimulation treatment; initial, including cortical mapping, motor threshold determination, delivery and management

Subsequent delivery and management, per session

Subsequent MT re-determination with delivery and management

CPT is a Registered Trademark of the American Medical Association
To schedule an appointment or for more information, contact:

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