

## Brain Stimulation – What Psychiatric Mental Health Nurses Need to Know

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## Disclosures

Mary Rosedale:

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- NYU College of Nursing Pless Center for Nursing Research
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## Objectives

### Objective 1 –

- Describe electromagnetic stimulation of the brain and how interventions differ in their degree of invasiveness, focality, efficacy, side effects, and mechanisms of action.

### Objective 2 –

- Examine the evidence base for Deep Brain Stimulation (DBS), Vagus Nerve Stimulation (VNS) Electroconvulsive Therapy (ECT), Magnetic Seizure Therapy (MST), Superficial Transcranial Magnetic Stimulation (TMS), Deep TMS, and Transcranial Direct Current Stimulation (tDCS)

### Objective 3 –

- Identify opportunities for PMH nurses in clinical practice, education, research, and health policy emphasizing collaboration with patients and their care-partners.

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## Neurobiology of Brain Stimulation

- Enhancement of serotonergic neurotransmission and activation of mesocortolimbic dopamine system with effects at levels: (a) transmitter release (b) receptor binding and (c) overall neurotransmission
- Long term down regulation of immune activation
- Increased BDNF and neuroplasticity

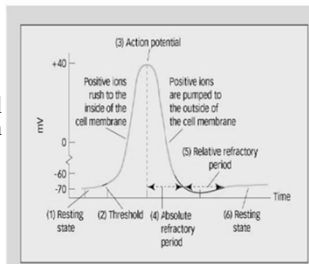
### CHOICE OF MODALITY DEPENDS ON:

- Severity of illness, extent of treatment refractory nature
- Patient preference
- Appropriate target of brain stimulation
- Dose- intensity of stimulation X duration of treatment

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## The Brain is an **Electrical** and Chemical Organ

- 100 billion neurons
- 100 trillion connections
- Interaction is a combination of electrical and chemical interaction
- An electrical impulse along an axon
- Excitatory or inhibitory
- Threshold = The level of stimulation needed to trigger an action potential

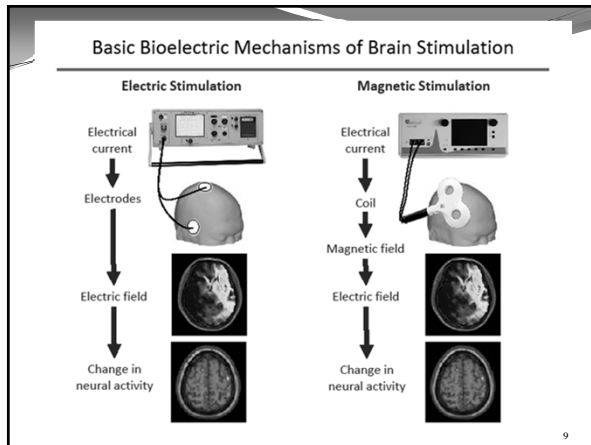
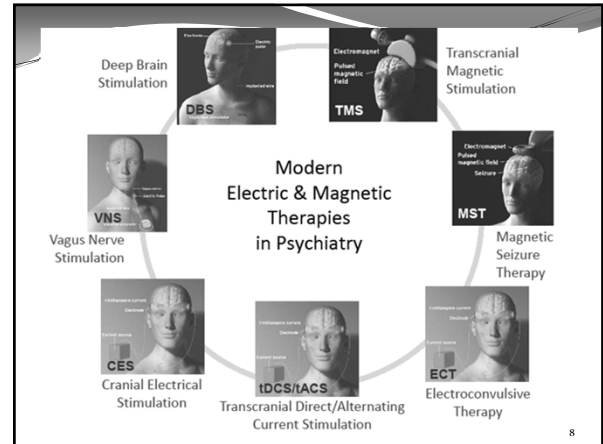


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## Inhibitory neurotransmission prevents excitation of the post-synaptic neuron

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	Psychiatric Drugs	Brain Stimulation
<b>Basic mechanisms</b>	Biochemical	Bioelectric
<b>Focality</b>	Unfocal (delivered through bloodstream) => side effects	Focal (delivered through electric field focused in brain) => potentially fewer side effects
<b>Speed of acute physiological response</b>	Slow (minutes to hours) => alters baseline concentration of chemicals	Fast (10s of microseconds) => can interact with brain dynamics (up to ~ 1,000 Hz)
<b>Ease of administration</b>	Easy (pills)	More involved: - Transcranial: 1 session ~ 10s of minutes; possibly in physician's office or hospital - Implanted: more invasive, chronic stimulation



Technique	Clinical Utility	Pros	Cons
ECT	Severe depression and schizophrenia	Highly effective (70-80% remission rate)	General anesthesia, seizure induction, cognitive side effects
TMS	FDA approved for depression, studies in other disorders	Non-invasive, no significant side effects	Modest efficacy; 24% response, 17% remission after 6 weeks
MST	Under study for depression	Reduced cognitive side effects compared to ECT	General anesthesia, seizure induction
VNS	Medication-resistant depression (FDA approved)	Less invasive than DBS	Requires surgery, limited efficacy, slow response: 16% remission after 12 months
DBS	Under study for treatment-resistant depression	Focal targeting of deep brain structures, works in some patients	Requires brain surgery, effectiveness under study
tDCS	Under study for depression, etc.	Non-invasive, no significant side effects, neuromodulatory effects	Randomized controlled trials support efficacy. Small sample sizes to date
CES	Claimed wide range of conditions	Non-invasive, no significant side effects	Efficacy & mechanisms unknown. Controlled trials lacking

## Electroconvulsive Therapy (ECT)

- ### Diagnoses that Respond to ECT
- Major Depression (with or without psychosis)
  - Bipolar – Depression and Mania
  - Schizoaffective
  - Early onset of Schizophrenia
  - Catatonia

### Diagnoses that Respond to ECT

- Neuroleptic Malignant Syndrome (NMS)
- Dementia with underlying mood disorder
- Pine Rest, McLean Hospital (Harvard University) and Mayo Clinic Research Published
  - *Short-term Efficacy and Cognitive Side Effects of Acute Electroconvulsive Therapy for Agitation and Aggression in Dementia*, International Journal of Geriatric Psychiatry, May 2014

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### Life Saving Treatment

- Actively Suicidal
- Rapid Response Needed

Suicide – (American Association of Suicidology)  
[www.suicidology.org](http://www.suicidology.org)

- Completed suicide: 41,149 cases reported in 2013 – 112.7 per day

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### Efficacy of ECT

- No trial has ever found an antidepressant medication regimen to be more effective than ECT
- As a first line treatment the response rates are 80 – 90%
- Among patients who have not responded to one or more adequate antidepressant trials the response rate remains substantial, 50-60%

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### Stimulus Electrode Placements

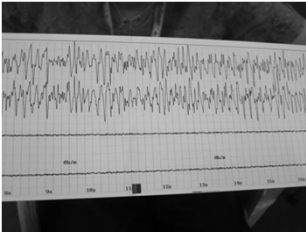
- Bi-temporal (bilateral)
  - Right Unilateral



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### Seizure Monitoring

- Seizure length typically 30-60 seconds
- Tonic/Clonic (Peripheral seizure)
- Brain activity (Central seizure)



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### ECT Treatments

- Acute Series
  - 3 times each week
  - Typically 6-12 treatments
  - Improvements seen after 4-6 treatments
- Maintenance
  - Weekly to monthly
  - Maintains the gains
  - Can prevent inpatient stays

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### Anesthesia

Anesthetic

- Brevital or Methohexital
- Etomidate or Amidate

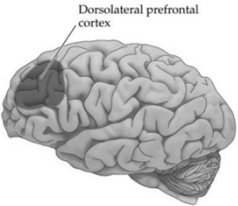
Muscle relaxant – Succinylcholine (Anectine)

- Depolarizing muscle relaxant
- Most common cause of muscle soreness

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### Mechanisms of Action

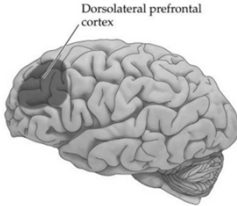
- Decreases frontal cortical connectivity
- Neurotransmitter theory
  - neurotransmitter function is restored from ECT by increasing the concentrations of neurotransmitters (acetylcholine or dopamine – needed to transmit impulses across a synapse)



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### Mechanisms of Action

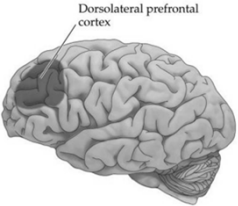
- Alters catecholamines – neurotransmitters and hormones and include epinephrine, norepinephrine, and dopamine
- Anticonvulsant theory – when the brain stops the seizure



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### Mechanisms of Action

- Anti-depressant
- Anti-manic
- Anti-psychotic
- Anti-parkinsonian
- Anti-convulsant



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### Benefits of ECT

➤ Improved mood	➤ Less agitation
➤ Increased pleasure	➤ Increased sexual interest
➤ More restful sleep	➤ More energy
➤ Better appetite	➤ Clearer thinking
➤ More positive attitude	➤ More hope

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### Potential Side Effects

- Headaches
- Muscle aches – caused by muscle relaxant
- Nausea
- Unsteady on feet
- Confusion
- Potential short-term and/or long-term memory loss

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### Contraindications

- No absolute contraindications
  - Space occupying lesion
  - Increased Intracranial Pressure
  - Recent MI or CVA
- High risk
  - Risk versus benefit
- Mortality
  - 1:10,000 patients
  - Less than for childbirth

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### Crucial Role of the PMH Nurse

- Nurse’s attitudes impact patients, family members and the community
- Staff’s attitudes impact patients, family members and the community

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### New Developments in ECT Administration

- Albuquerque, New Mexico
- Northhamptom, England

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### Patient Education

- ECT Educational Websites
  - <https://www.isen-ect.org/>
  - Mayo Clinic
  - Universities – Duke, University of Michigan, Loma Linda, etc.
- ECT Video
  - <http://geiselmed.dartmouth.edu/mood>
  - Mayo Clinic
- ECT Pamphlets
  - <http://www.channing-bete.com>
  - Carol Kivler – Courageous Recovery



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### Summary of ECT

- ECT is a very safe and effective treatment
- ECT can be a life saving treatment
- Patient’s response to ECT is typically quick usually about 4-6 treatments
- ECT can keep patients out of the hospital
- ECT improves patients’ quality of life

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### Transcranial Magnetic Stimulation (TMS) Therapy

- TMS is a non-invasive treatment for Major Depressive Disorder (MDD) in adult patients
- FDA approved in October 2008 for MDD with one failed antidepressant trial

### TMS Therapy

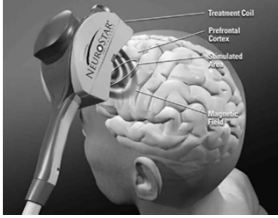
- FDA approved in April 2014 for MDD for those who have failed to benefit from any number of antidepressant trials
- Off-label uses: treatment of anxiety disorders, Bipolar Disorder, Post-Traumatic Stress Disorder, chronic pain, fibromyalgia, eating disorders, and Parkinson's Disease

### TMS Therapy

- Stimulates cortical neurons by delivering magnetic pulses to a specific area of the brain
- Utilizes a magnetic field generated by a treatment coil applied to the head, usually 1.5–3.0 tesla
- Neuronetics TMS “NeuroStar” machine generates 0.5 tesla
- For comparison, 3.0 T is the strength of magnetic field generated by most medical Magnetic Resonance Imaging (MRI) systems

### Transcranial Magnetic Stimulation (TMS) – What is it?

- Electromagnetic induction described by Michael Faraday in 1839 – magnetic field induces a perpendicular electric current.
- TMS uses magnetic pulses to *induce* a current in the brain instead of *applying* a current as in ECT



1. Faraday M. In: *Experimental Research in Electricity*. Vol 1. London Quaritch; 1839:1-15

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### TMS Safety Profile

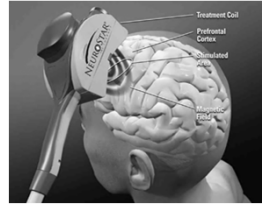
- No seizures in pre-marketing studies (10,000 active treatments) and recent Multisite NIMH study. Seizures are rare, but have been reported.
- No systemic side effects such as weight gain, sexual dysfunction, nausea, etc.
- No adverse effect on cognition
- Most common adverse events were headache and scalp discomfort
- <5% of patients discontinued due to adverse events in pre-marketing studies

Janicak PG et al. *J Clin Psychiatry*. 2008;69(2):222-232.

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### How TMS Works

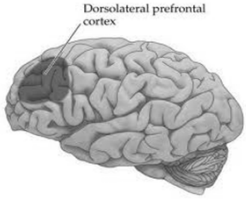
- Electric energy within insulated coil induces magnetic fields
- Magnetic fields penetrate the cranium 1.5- 2.0 cm below the device
- Magnetic fields induce electric current in the brain
- Results in depolarization of nerve cells causing release of neurotransmitters



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### Dorsolateral Prefrontal Cortex (DLPFC)

TMS produces its effect through electrical stimulation of the DLPFC; this is the area of the brain believed to be responsible for regulating mood.



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### Early Transcranial Magnetic Stimulation



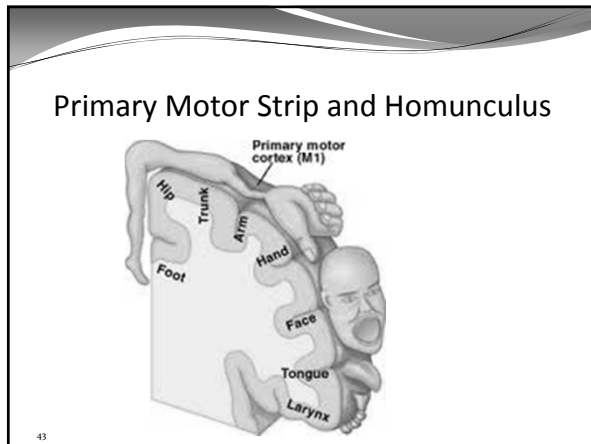
Barker & Jalilous, 1985

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### Identifying TMS Treatment Location

- Coil is applied to the Primary Motor Cortex to initiate a thumb twitch response; this is called the Motor Threshold (MT)
- MT determines the energy required to effectively treat depression and helps identify the location of the DLPFC
- Coil is placed 5.5 cm anterior to the location of the MT

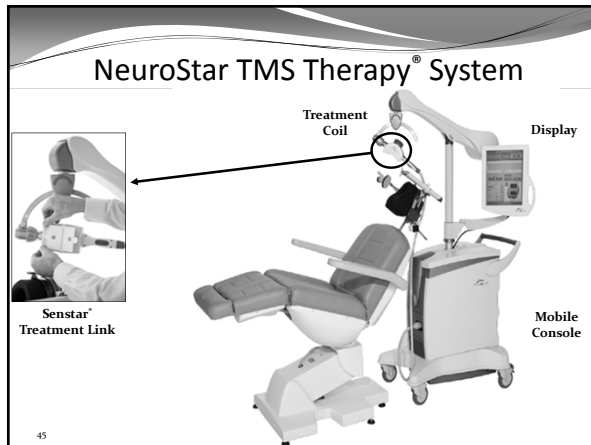
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### TMS Administration

- TMS sessions: 1 per day for 4-6 weeks (typically Monday through Friday)
- Typical series is 30 treatments
- Treatments last 25 - 40 minutes
- Patient positioning & Motor Threshold is determined
- Recommended Intensity: 120% of MT
- Frequency: pulses per second (10 Hz or 1 Hz)
- Treatment train: 4 seconds of stimulation with 26 seconds of no stimulus; 3000 total pulses per treatment

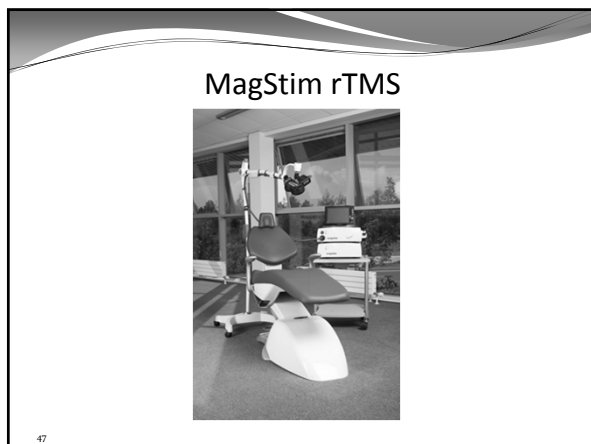
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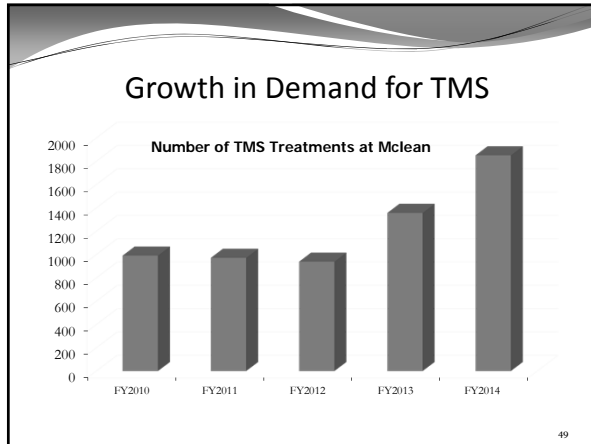
### Brainsway TMS System

- Deep TMS (dTMS)
- Magnetic field penetrates 5.5-8.0 cm

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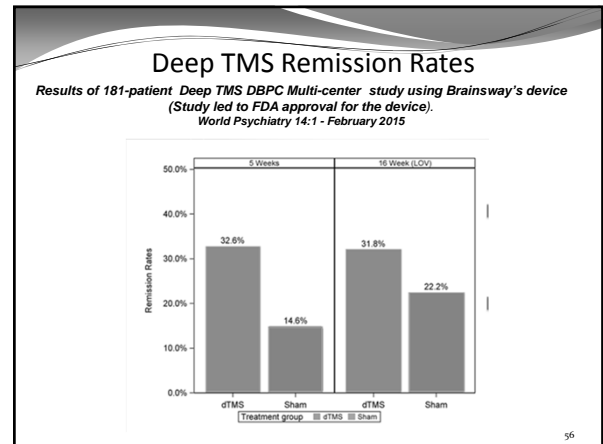
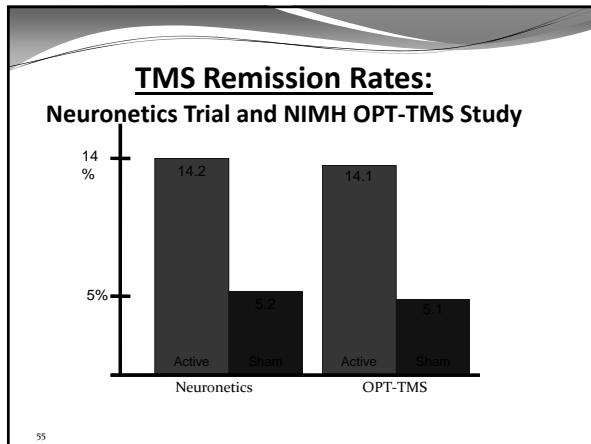
- ### Patient Selection for TMS
- Patients with MDD who have failed trials of antidepressant medications
  - Patients who have been carefully screened for any of the absolute contraindications to receiving TMS
  - Patients who are willing and able to commit to treatments five days a week for 4-6 weeks
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- ### Absolute Contraindications:
- Seizure disorder or history of seizures (except those induced by ECT)
  - Intracranial devices
  - Carotid or cerebral stents
  - Space occupying brain lesions
  - Evidence of increased intracranial pressure
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- ### Relative Contraindications
- Dementia & other degenerative neurological conditions
  - Unstable medical conditions
  - Chronic or acute psychotic disorders
  - Serious co-morbid psychiatric conditions
  - Implantable automatic defibrillator or cardiac pacemaker
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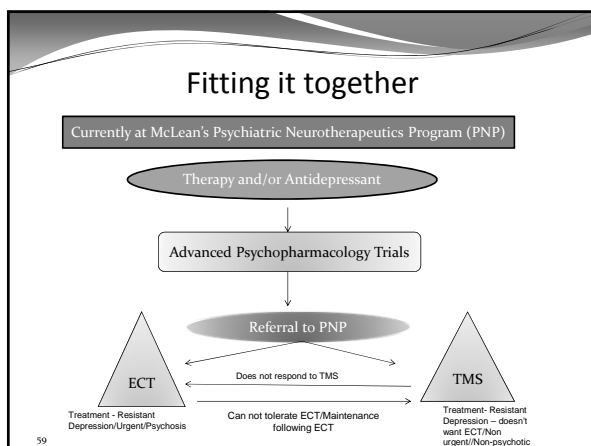
- ### Clinical Considerations
- Performed as an outpatient or inpatient procedure
  - Patient is awake, alert during treatment
  - Treatment lasts 25 - 40 minutes, patient resumes normal activity afterwards
  - Many TMS patients continue to take psychotropic medications
  - Many insurance companies provide TMS coverage, either as part of their policy or on a case-by-case basis
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- ### TMS Side Effect Profile
- Common Side Effects
- Scalp discomfort, tenderness at coil placement site
  - Headache, may be managed with an over the counter analgesic
  - Facial pain, muscle twitching
- Rare Side Effects
- Risk of generalized seizure: 1 in 30,000 treatments or 0.003%
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- ### TMS Roles
- TMS machine is a class II device requiring a prescription
  - Attending psychiatrist oversees initial patient MT determinations, treatment parameter definitions, & overall TMS treatment course planning
  - Ideally, treatment is administered (or supervised) by a RN

- ### Role of the PMH Nurse in TMS
- Assessing
  - Administering psychiatric scales
  - Administering treatments within prescribed parameters
  - Monitoring
  - Coordinating care with outpatient providers
  - Crisis intervention as needed (psychiatric and medical)



- ### TMS Manufacturers
- Brainsway (Israel), [www.brainsway.com](http://www.brainsway.com)
  - Neuronetics Inc., [www.neuronetics.com](http://www.neuronetics.com)
  - MagStim [www.magstim.com](http://www.magstim.com)

### TMS Manufacturers

- CR Tech (Seoul, South Korea)
- Magstim Company, Ltd. (Whitland, UK) [www.magstim.com](http://www.magstim.com)
- MAG&MORE GmbH, (Munich, Germany)
- Mcube Technology Co., Ltd. (Seoul, South Korea)
- Medtronic Dantec NeuroMuscular (Skovlunde, Denmark) [www.medtronic.com](http://www.medtronic.com)
- Neuralieive (California, USA) [www.neuralieive.com](http://www.neuralieive.com)
- Nexstim (Finland) [www.nexstim.com](http://www.nexstim.com)
- Schwarzer (München, Germany) [www.schwarzer.net](http://www.schwarzer.net)

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4. Dell'Osso B, Camuri G, Castellano F, Vecchi V, Benedetti M, Bortolussi S, Altamura AC. Meta-review of meta-analytic studies with repetitive transcranial magnetic stimulation (rTMS) for the treatment of major depression. *Clinical Practice & Epidemiology in Mental Health* 2011; 7: 167-177.
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7. Higgins ES, George MS. *Brain Stimulation Therapies for Clinicians.* Washington, DC: American Psychiatric Publishing, Inc., 2009

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### Magnetic Seizure Therapy

**Investigational**  
 Magnet-induced stimulus  
 High Intensity  
 Target "antidepressant regions"  
 Fewer side effects -no direct electrical stimulation of medial temporal lobe structures such as the hippocampus, which are implicated in ECT-related memory impairment  
 3 sessions/week  
 Same as ECT  
     Anesthesia  
     Tonic clonic seizure  
     Monitor EEG, vitals

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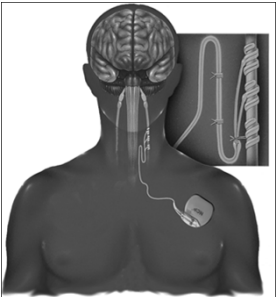
### Magnetic Seizure Therapy for Unipolar and Bipolar Depression: A Systematic Review

- 8 studies included
- As effective as ECT in inducing generalized tonic-clonic seizures
- Effective treatment for depressive episodes, with response rates ranging from 40%- 60% and remission rates ranging from 15% - 30%
- On human subjects, reorientation time after MST ranges from 2 - 8 minutes to 8 minutes, while it takes from 18 minutes -26 minutes after ECT. Other cognitive functions, such as retrograde and anterograde memory, language, and praxis, seem to be unaffected by MST
- Future research, with larger samples, of double-blind design, and more consistent methods will allow for more statistic power and better understanding of the technique

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### Vagus Nerve Stimulation (VNS)

- FDA approved for epilepsy; FDA approved for TRD July, 2005
- Implanted in over 30,000 patients worldwide
- Pulse generator implanted in left chest wall area, connected to leads attached to left vagus nerve
- Mild electrical pulses applied to CN X for transmission to the brain



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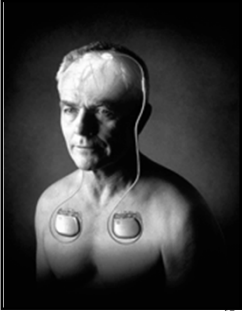
### Systematic review and meta-analysis of VNS in the treatment of depression: variable results based on study designs

- 14 studies included
- Meta-analysis of efficacy for uncontrolled studies showed a significant reduction in scores at the HamD and percentage of responders was 31.8% ([23.2% to 41.8%],  $P < 0.001$ ).
- The RCT (N= 235 patients) reported no statistically significant differences between the active intervention and placebo groups (OR = 1.61 [95%CI 0.72 to 3.62];  $P = 0.25$ )
- Insufficient data available to describe VNS as effective for treatment of depression. In addition, it cannot be ruled out that the positive results observed in the uncontrolled studies might have been mainly due to a placebo effect

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### Deep Brain Stimulation

- FDA Approved for Parkinson's and Tremor
- Investigational for OCD, TRD
- Stereotactic Target from MRI
- Two chest-wall Pulse Generators
- Burr holes in skull for electrode placement
- Stimulation parameters programmed by computer, through "wand"
- This information concerns a use that has not been approved by the U.S Food and Drug Administration



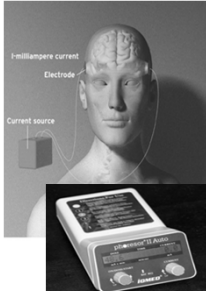
Medtronic, 2013

### Transcranial direct current stimulation for Major Depression: an updated systematic review and meta-analysis

- 7 RCTs (n = 259) included, most with small sample sizes that assessed tDCS as monotherapy or add-on therapy.
- Active vs. sham tDCS was significantly superior for all outcomes (g = 0.37; 95% CI 0.04-0.7; ORs for response and remission were, respectively, 1.63; 95% CI = 1.26-2.12 and 2.50; 95% CI = 1.26-2.49). No predictors of response were identified, possibly owing to low statistical power.
- Active tDCS was statistically superior to sham tDCS for the acute **depression** treatment. Further RCTs with larger sample sizes and assessing tDCS efficacy beyond the acute **depressive** episode are warranted.

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### Transcranial Direct Current Stimulation (tDCS) in HIV-Infected, Depressed Persons



tDCS was an Safe, effective and tolerable treatment in 7 HIV patients with co-morbid major depression and associated with significant (P < .05) decreases in HAMD-24 and MADRAS scores

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### Systematic Review: Alternating current cranial electrotherapy stimulation (CES) for depression

- Low intensity electrical current administered through the use of a small, portable electrical device, has been reported to have efficacy in the treatment of depression with minimal adverse effects.
- Investigated the scientific evidence regarding the efficacy and safety of CES in treatment of acute depression compared to sham, or simulated, CES treatment. There are insufficient methodologically rigorous studies of CES in treatment of acute depression. There is a need for double-blind randomized controlled trials of CES in the treatment of acute depression.

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### Psychiatric Nursing and Brain Stimulation: Back to the Future

Pictures Provided by Medical University of South Carolina



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