The Significant Promise of Therapeutic Neuromodulation: Implications for Psychiatric Mental (PMH) Health Nursing

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Objectives

1. Describe how neuromodulation aims to regulate neurotransmitters and downstream neurochemical cascades;
2. Examine the safety and efficacy of DBS, VNS, ECT, deep TMS, TMS and tDCS;
3. Identify opportunities for advancing the science of neuromodulation in PMH nursing and nursing research.

The Brain as 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

Brain Stimulation Techniques

• Electroconvulsive Therapy (ECT)
• Vagus Nerve Stimulation (VNS)
• Repetitive Transcranial Magnetic Stimulation (rTMS)
• Deep Brain Stimulation (DBS)
• Epidural Cortical Stimulation (EpCS)
• Transcranial Direct Current Stimulation (tDCS)
Survey of the major neurotransmitters

Inhibitory neurotransmission prevents excitation of the postsynaptic neuron

Mayberg, HS, 1999

Drevets, WC, 2001
Depression
- Cerebral blood flow & Metabolism
- Hippocampal volume
- Serotonin
- Dopamine

Neurogenesis & Neuroplasticity
- Neuroplasticity – The ability of the neural pathways and synapses to adapt to stimuli by reorganizing structurally and functionally.
- Neurogenesis - The birth of new neurons mostly known to occur in the dentate gyrus of the hippocampal formation.

ECT
- Plasma prolactin levels
- Thyrotropin-releasing hormone (TRH)
- TRH-receptor function
- Brain-derived neurotrophic factor (BDNF)

TMS
- Cerebral blood flow in the prefrontal & paralimbic areas
- Dopamine
- Serotonin
- Thyroid-stimulating hormone (TSH)
- Glutamate levels
- GABA

Electroconvulsive Therapy (ECT)

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Diagnoses

- Major Depression (+/- psychosis)
- Bipolar – Depression and Mania
- Schizoaffective
- Catatonia

Other diagnoses

- Neuroleptic Malignant Syndrome
- Dementia with underlying mood disorder
- Current research project –
  - Short-term Efficacy and Cognitive Side Effects of Acute Electroconvulsive Therapy for Agitation and Aggression in Dementia

Life Saving Treatment

- Actively Suicidal
- Rapid Response Needed

Suicide – (National Institute of Mental Health, Jan. 11, 2011)

- The overall rate was 11.3 suicide deaths per 100,000 people.
- An estimated 11 attempted suicides occur per every suicide death.
- Children ages 10 to 14 — 0.9 per 100,000
- Adolescents ages 15 to 19 — 6.9 per 100,000
- Young adults ages 20 to 24 — 12.7 per 100,000
- Older adults ages 65 and older – 14.3 per 100,000
- Older non-Hispanic white males 85 and older – 47 per 100,000

Improvements in ECT

- Medications
  - Anesthesia
  - Muscle Relaxant
- Oxygenation
  - Administration of oxygen
  - Monitor oxygen saturation

Type of electricity – brief pulse wave
- Seizure monitoring
- Stimulus dosing
- Ultra brief pulse
Stimulus Electrode Placements

- Bi-temporal
- Right Unilateral
- Bifrontal

Seizure Monitoring

- Seizure length 30-60 seconds
- Tonic/Clonic (Peripheral seizure)
- Tachycardia
- Electroencephalogram (EEG) (Central seizure)

ECT Treatments

- Acute Series
  - 3 times each week
  - Typically 6-12 treatments
  - Improvements seen after 4-6 treatments
- Maintenance
  - Weekly to monthly
  - Can prevent inpatient stays
- 80% of patients relapse after ECT with no follow up of medications or maintenance ECT

Seizure Threshold

Medications that can change seizure threshold

- Lithium
- Benzodiazepines
- Mood stabilizers
- Antipsychotics

Seizure Threshold

Other influences on seizure threshold

- Age
- Gender
- Electrode placement
- Hyperventilation
- Dehydration
- Sleep

Seizures

- Parasympathetic discharge
- Sympathetic discharge
- Potential rebound parasympathetic discharge
### Anesthesia

Anesthetic
- Brevital or methohexital
- Etomidate

Muscle relaxant – succinylcholine (anectine)
- Depolarizing muscle relaxant
- Most common cause of muscle soreness

### Potential Mechanisms of Action

- Decreases frontal cortical connectivity
- Neurotransmitter theory
- Anticonvulsant theory

### Benefits of ECT

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

### Potential Side Effects

- Headache and muscle aches
- Nausea
- Unsteady on feet
- Confusion
- Potential short-term and/or long-term memory loss

### Contraindications

- No absolute contraindications
- High risk
  - Risk versus benefit
- Mortality
  - Less than for childbirth

### Pre-ECT Workup

- Psychiatric referral
- Basic Metabolic Profile
- Electrocardiogram
- History & Physical—medical clearance
- Inpatient versus Outpatient
- Risk/Benefit Ratio
- Education
- Informed Consent
ECT Procedure
- Patient and Family rating scale
- Assessment of patient
- Intravenous line placement
- Anesthesia and muscle relaxant
- Brief electrical stimulus
- Monitor seizure activity
- Post Anesthesia Care Unit
- Vitals stable – discharge

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Transcranial Magnetic Stimulation (TMS) Therapy
- Indicated for the treatment of Major Depressive Disorder (MDD) in adult patients
- Is non-invasive, generally well tolerated (Barker & Jalinous, 1985)
- Utilizes a magnetic field generated by a treatment coil applied to the head, usually 1.5 - 3.0 tesla (Higgins & George, 2009)
- Neuronetics TMS machine generates 0.5 tesla (Neuronetics, Inc., 2010)

TMS Therapy
- For comparison, 3.0 T is strength of magnetic field generated by most medical Magnetic Resonance Imaging (MRI) systems in use (Higgins & George, 2009)
- TMS produces its effect through electrical stimulation of the area of the brain believed to be responsible for mood (Neuronetics, Inc., 2010)

Early Transcranial Magnetic Stimulation

How Does TMS work?
Picture from Manufacturer: Neuronetics
- Electric energy within insulated coil induces magnetic fields
- Magnetic fields penetrate the cranial 1.5-2.0 cm below the device
- Magnetic fields induce electric current in the brain
- Which leads to depolarization of nerve cells causing release of neurotransmitters (Higgins ES, George MS, 2009; Neuronetics, Inc., 2010)

Identifying TMS Treatment Location
Coil applied to the Primary Motor Cortex area of the brain to elicit thumb twitch
Called Motor Threshold (MT)
MT determines energy required to effectively treat depression, as well as helps identify location of Dorsolateral Prefrontal Cortex (DLPFC)
Dorsolateral Prefrontal Cortex (DLPFC)

Area of the brain believed to be responsible for regulating mood

(Baeken C, De Raedt R, 2011; Dell’Osso, et al., 2011)

TMS Manufacturers

- Brainsway (Israel), [www.brainsway.com](http://www.brainsway.com)
- 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)
- Neuralieve (California, USA) [www.neuralieve.com](http://www.neuralieve.com)
- Neuronetics Inc. [www.neuronetics.com](http://www.neuronetics.com)
- Nexstim (Finland) [www.nexstim.com](http://www.nexstim.com)
- Schwarzer (München, Germany) [www.schwarzer.net](http://www.schwarzer.net)

FDA Labeling

NeuroStar® TMS Therapy System is a prescription device under 21 CFR Part 801.109 that is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode.

(Neuronetics, Inc., 2010)

NeuroStar TMS Therapy® System
(Picture from Manufacturer: Neuronetics)

TMS Administration

- Recommended intensity: 120% of MT
- Frequency: pulses per second (10 Hz or 1 Hz)
- Stimulation time: 4 seconds, with 26 second rest time; 3000 total pulses per treatment
- TMS sessions: 1 per day for 4-6 weeks.

Patient Selection for TMS

- Pt with MDD who has failed one trial of antidepressant at or above minimally effective dose, for a minimal duration (at least 4 weeks) in the current episode of MDD

- Pt has no history of seizures, no ferromagnetic metal objects or shrapnel above the shoulders, no implantable medical devices; for instance:
Patient Selection for TMS Con't

- Pacemakers, or other implanted physiologic devices; coronary artery stents, aneurysm coils and clips; cochlear implants are contraindicated for use of TMS
- No metallic tattoos; permanent makeup should be > 30 cm from coil

Clinical Considerations

- Performed as an in-/outpatient procedure
- Patient is awake, alert during treatment
- Treatment lasts about 40 minutes, patient resumes normal activity afterwards
- Many TMS patients continue to take psychotropic medications
- Insurance may cover TMS on case-by-case basis

Clinical Considerations

Common Side Effects

- Scalp discomfort, tenderness at coil placement site
- Headache, may be managed with OTC analgesic of choice
- Facial pain, muscle twitching

Response, Remission, Non-Response Rates for TMS pts at WRNMMC

- **Response**: 50% reduction in baseline mood scale score (PHQ-9, QIDS-SR): 44.4%. Of those who responded,
- 3 of 4 met criteria for full remission of MDD symptoms
- **Remission**: Full resolution of depressive symptoms (PHQ-9 score < 5, QIDS-SR < 6)
- **Non-Response** rate at WRNMMC after 20+ TMS sessions: 44.4%

TMS: “Who does What?”

- TMS machine is a class II device prescribed by MD, NP
- Each state regulates prescriptive authority which includes nurse practitioners
- Providers with prescriptive authority dictate the dose of TMS, other operators may administer TMS treatment
- Ideally, person administering TMS is medically-trained and able to manage a seizure
Why PHM-RN Role in TMS is Important

- Monitor for patient safety and effective treatment
- Allows for close, daily patient assessment
- Coordinate care with outpatient providers
- Crisis intervention as needed

References


Deep & Cortical Brain Stimulation
(Pictures from Manufacturers: Medtronic, NeuroPace)

Bilateral Epidural Prefrontal Cortical Stimulation for TRD
(Pictures Provided by Manufacturer: Synergy)

Cognition, executive control and integration of emotion: 2 complimentary networks
(Picture Provided by Manufacturer: Synergy)
Overlapping Paradigm Shifts in Nursing and Brain Stimulation

- 50 years is needed to make a paradigm shift
- In the past 6 decades, Nursing has been transformed from an occupation where nurses do to and for patients, to a profession where nurses work with patients
- For more than 7 decades, nurses have provided specialized care for ECT patients
- Brain stimulation therapies are a new therapeutic class and Psychiatric Nursing field

tDCS for Depression

(Rigonnati et al., 2008 & Fregni et al., 2006)

Figure 2: Effects of tDCS over DLPFC as compared with sham and antidepressant fluoxetine on depression relief in 42 patients with Major Depression.

Safety, Tolerability and Feasibility of tDCS for HIV+ Persons Racial and Ethnic Minorities with MDD

- 10 sessions over PFC
- Phoressor II 850 PM using 2 electrodes (36cm²) placed over F3 position of EEG 10-20 system and the contralateral supraorbital region.
- Recruit racial/ethnic minorities
- HamD24 and MADRAS
- Cytokine assays
- Analyze characteristics of completers/ non-completers
- Conduct qualitative interviews to incorporate subject input in future patient-centered treatment protocols
- Open label, 2 week block of tDCS

Transcranial Direct Current Stimulation 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

A Treatment Wish List

- An evidence-based treatment for depression and pain
- Focus and dose that can be personalized
- Faster onset than medications
- Acceptable to those who cannot tolerate medications due to side effects, med interactions and comorbidities
- Adjuvant treatment for those reporting partial relief from other treatments (safely combined/optimized response)
- Feasible for patients with low performance status (minimal patient effort or attention)
- Clinically tested in racial and ethnic minorities
- Well tolerated, brief, safe, easy to administer and inexpensive
There is a very specific kind of pain to depression and it became less vicious. It was not that pain changed; the perception of pain changed. (Rosedale, Lisanby & Malaspina, 2009. Research Brief: The structure of the lived experience for persons having undergone TMS for depression treatment. Journal of the American Psychiatric Nurses Association, 15(5), 333-337.)

Key Issues: Reclassification of ECT by FDA and APNA’s Position Statement

- ECT as evidence-based practice
- Unparalleled efficacy of ECT and dangers of limiting access
- Evolution of ECT and Brain Stimulation
- Misinformation and stigma of psychiatric conditions and treatments
- Key Issues at FDA hearings
- APNA’s Vital Leadership Role and Position

How History of Brain Stimulation Shapes Psychiatric Nursing’s Future

- Advancing Evidence-based practice
- Combining Psychotherapeutic Treatments
- Combining Qualitative and Qualitative Approaches
- Treating new populations
- Advocating for Our Patients
- Influencing Public Policy

Life Long Neurogenesis:

- Olfactory System
- Hippocampus
- Olfactory Epithelium → Culture Olfactory Neurons → Gene Expression Studies → Potential for Stem cells
- Hippocampal Dentate Gyrus → Coronal and sagittal 7T → 100 micron cell layer

APA ECT Task Force: APNA Consultation on Nurse’s Role

Second edition (2001)

- Third edition (2013)
- Evidence-based Nursing Practice and APN roles
- Accurately representing the wealth of psychiatric nursing expertise and the contributions of nursing profession

Translational Neuroscience Research

- Clinical Research
- Epidemiology
- Basic Science
- Animal Models
- Neurobiologyfoundation.org
Psychiatric Nursing and Brain Stimulation: Back to the Future

Pictures Provided by Medical University of South Carolina