Therapeutic Brain Stimulation: Past, Present, Future and Critical Issues for Psychiatric-Mental Health Nurses

American Psychiatric Nurses Association
25th Annual Conference
October 19, 2011
Anaheim, California
Cindy L. Brown, BSN, RN
Amy J. Rust, BSN, RN
Berry S. Anderson, PhD, RN
Mary Rosedale, PhD, PMHNP-BC
Gerald Georgette, RN

Objectives

- Explore how brain stimulation has historically been part of psychiatric nursing and how it will help shape psychiatric nursing’s future
- Examine the safety and efficacy of VNS, DBS, EpCS, TMS, and tDCS
- Discuss reclassification of ECT by the FDA and APNA’s position statement

Disclosures

- Grant and Research Award funding (Rosedale): American Psychiatric Nurses Foundation (APNF), NYU Pless Center for Nursing Research, Edith L. Fisch Award for Innovation in Neurostimulation

Brain Stimulation in the News

- How a Junkie's Brain Helps Parkinson's Patients
- Darpa Wants Remote Controls to Master Troop Minds
- Brain 'Pacemaker' TICKLES Your Happy Nerve
- This is Your Brain on Electricity
- Shock Therapy Loses Some of Its Shock Value

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

A New Paradigm and New Ways of Thinking

- Psychotherapy as a biological treatment
- The polygenic nature of illness and epigenetics
- Sequencing and combining psychotherapy, medication and brain stimulation to personalize treatment
- Life-long neurogenesis
- Brain as electrical and chemical organ with connected regions that can therapeutically be modulated
New Ways of Thinking-Psychotherapy is a Biological Treatment

- Increases in pCREB early in the course of psychotherapy (Koch et al., 2009) associated with treatment response
- Future research needed to explore the interaction of pharmaco-nutraceutical-psychotherapy and brain stimulation using biological parameters predictive of treatment response

Epigenetics and Different Aspects of Life

- Development of multicellular organism
- Environment-organism interaction
  - For example: Parental Age, trauma, nutrition supplements and environmental toxins
- Pathogenesis of diseases

The Double Helix

Watson and Crick, 1953

The Interactome

Complex Molecular interaction networks

“The Double Helix
Watson and Crick, 1953

“We have found the secret of Life”

Fine tuning our behavior and survival to the expected environment

Life Long Neurogenesis: Olfactory System

Hippocampus

Interplay between different regions

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
The Science is Moving at Accelerated Rate: Changing Practice and Knowledge Development

Non-procedural, Evidence-based Factors Changing Role of ECT Nurse

- Expanded roles for nursing (i.e., nurse anesthetist and nurse practitioner)
- Movement from inpatient to outpatient treatment (continuation and maintenance)
- More complex and ill patients requiring increased monitoring and more clinically sophisticated practice (i.e., In ICU)
- Greater regulation
- Advent of novel neuromodulation methods
- Greater attention to treatment-resistance

Safety and Efficacy of ECT

Evidence-based treatment Advances changing the role of ECT Nurse:

- Electrode placement
- Stimulus dosing
- Seizure threshold titration
- Changes in wave form and pulse width
- Use of physiological monitoring
- Choice of anesthetic agents
- Use of "time outs"

Magnetic Seizure Therapy: Decreased Depression Severity on Clinician Rated Measure

<table>
<thead>
<tr>
<th>Group</th>
<th>HRSD Baseline</th>
<th>HRSD End</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>30</td>
</tr>
</tbody>
</table>

Cyberonics, Inc., Houston, TX
Vagus Nerve Stimulation

- Battery life of the pulse generator is between 1-6 years depending on strength, length, and frequency of signal
- Proposed mechanisms of action include alteration of norepinephrine release to locus coeruleus and elevated levels of inhibitory GABA

FDA Approved Indications for VNS Therapy™

- On July 16, 1997, the FDA approved the NCP System (the predecessor to the VNS Therapy System) for use "as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over twelve (12) years of age with partial onset seizures that are refractory to antiepileptic medications."
- On July 15, 2005, the FDA approved the VNS Therapy System "for the adjunctive long-term treatment of chronic or recurrent depression for patients eighteen (18) years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments."

What is TMS? (Transcranial Magnetic Stimulation)

- Electric energy within insulated coil induces MRI-strength magnetic fields
- Magnetic fields pass unimpeded through the cranium for 2-3 cm
- In turn inducing an electric current in the brain
- This stimulates the firing of nerve cells and the release of neurotransmitters

Transcranial Magnetic Stimulation

Approximate Depth Limit of Direct Stimulation with Current TMS Coils
TMS Manufactures

- Brainsway (Israel), www.brainsway.com
- CR Tech (Seoul, South Korea)
- Magstim Company, Ltd. (Whitland, UK) www.magstim.com
- MAG&MORE GmbH, (Munich, Germany)
- Mcube Technology Co., Ltd. (Seoul, South Korea)
- Medtronic Dantec NeuroMuscular (Skovlunde, Denmark) www.medtronic.com
- Neuralieve (California, USA) www.neuralieve.com
- Neuronetics Inc. www.neuronetics.com
- Nexstim (Finland) www.nexstim.com
- Schwarzer (München, Germany) www.schwarzer.net

Applications of TMS

- Brain Mapping
- Measuring cortical excitability in disease and in response to drugs
- Depression, Bipolar Disorder, Schizophrenia, OCD, Parkinson’s disease, Tourette’s Disorder, and Pain
- Sleep deprivation
- Migraines

FDA Labeling

NeuroStar® TMS Therapy System as 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.

TMS Administration

- Location- prefrontal cortex for depression treatment. (5 cm rule?)
- Intensity- % of motor threshold (120%)
- Frequency- pulses per second (10 Hz)
- Trains of stimulation- duration, inter-train Interval, & # of trains. (4 seconds on, 26 seconds off, 75 trains)
- TMS sessions- 1 per day for 4-6 weeks.
How does TMS treat depression?

- **Hormonal** - hits hypothalamic-pituitary-adrenal circuit, resets thyroid, CRH, cortisol
- **Cortical Governing** - rebalances relationship between cortex and limbic
- **Anticonvulsant** - mimics brain’s antiseizure surveillance mechanism with local transmitter changes (GABA)

Safety of TMS

**Side Effects**
- Mild Headache
- Mild Discomfort at sight of stimulation
- Temporary increase in auditory threshold (without ear plugs)
- Induce Mania (rare)
- Induce Seizure (rare)

**Contraindications to TMS**
- cochlear implant
- aneurysm clips
- brain electrodes
- ferromagnetic material in their head or neck
- stroke
- head trauma

MT Site and Treatment Site

Starting Point

Treatment Site

Vertex

Homunculus

20 Hz rTMS

1 Hz rTMS

Speer et al Biol Psych 2000

MUSC, Anderson, BS

Safety of TMS
TMS “Who does What?”

- TMS machine is a class II device for prescription use.
- Each state regulates prescriptive authority which includes nurse practitioners.
- Physicians or clinicians with prescriptive authority dictate the dose of TMS, but other clinicians usually administer the TMS treatment. The person administering TMS is medically trained and able to manage a seizure.

TMS Clinical Patients

- Performed most often as an outpatient procedure
- Awake, alert, oriented during treatment
- Treatment lasts just under 40 minutes
- Able to go about daily activities immediately afterwards
- Most insurance covers TMS only on a case-by-case basis
- In clinical practice many TMS patients continue to take psychotropic medications

TMS Training

- TMS training certification courses
  - ISN sponsored TMS training, May 2011 in Honolulu, Hawaii
- TMS related educational opportunities for nurses

PHM-RN Role in TMS

- Administer daily treatment
- Daily patient assessments
- Therapeutic interventions
- Continuous monitoring during treatment
- Coordinate care with outpatient providers
- Crisis intervention as needed

TMS Remission Rates: Neuronetics Trial and NIMH OPT-TMS Study

<table>
<thead>
<tr>
<th></th>
<th>Neuronetics</th>
<th>OPT-TMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>14.2%</td>
<td>14.1%</td>
</tr>
<tr>
<td>Active Sham</td>
<td>5.1%</td>
<td>5.2%</td>
</tr>
<tr>
<td>5%</td>
<td>14%</td>
<td></td>
</tr>
</tbody>
</table>

PHM Remission Rates: Neuronetics Trial and NIMH OPT-TMS Study

Healing patients with TMS

Photo courtesy of Rush University Medical Center, TMS Center
**Deep & Cortical Brain Stimulation**

- NeuroPace
- Medtronic

**Epidural Prefrontal Cortical Stimulation**

- Electrodes
- Dorsal cortical
- Electrical pulse
- Implanted pacemaker

**Work to prepare for EpCS study**

- ECT: Prefrontal - limbic governance
- Post-ictal prefrontal deactivation
- "It's not the seizure, but the Brain’s response to the seizure”
  - GABA modulation
- Hypothesis: Chronic modulation for relapse prevention

**Transcranial Direct Current Stimulation**

- Noninvasive technique for modulation of cortical excitability
- Low intensity direct current applied with 2 electrodes penetrates the scalp to the brain influencing neuronal excitability and modulating firing rates of individual neurons

**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.

Legend: Effects of fluoxetine were substantially delayed; tDCS had immediate effect that was stable for the entire observed period (6 weeks). T1: 2 weeks after tDCS delivered (5 sessions) in one study group or fluoxetine started in another study group; T2: 4 weeks; T3: 6 weeks after the study treatment.

**Transcranial Direct Current Stimulation in HIV-Infected, Depressed Persons**

- 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 (Rosedale & Knotkova, in review)
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/optimizing 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)

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

Translational Neuroscience Research

- Clinical Research
- Epidemiology
- Basic Science
- Animal Models

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

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

- Third edition (2013)
- Evidence-based Nursing Practice and APN roles
- Accurately representing the wealth of psychiatric nursing expertise and the contributions of nursing profession
Psychiatric Nursing and Brain Stimulation: Back to the Future