Next Generation Treatments for Resistant Depression:
The UMN Interventional Psychiatry Approach

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Disclosure information

● I have no financial relationships to disclose
● I will discuss off-label use of ketamine in this presentation
Learning objectives

- Describe an innovative care model designed for the comprehensive management of treatment-resistant depression, integrating interventions such as ketamine, TMS, ECT, VNS, advanced pharmacotherapy, and evidence-based psychotherapy.

- Describe the optimal clinical strategies for integrating interventional psychiatric treatments into the management of treatment-resistant depression.

Depression is the leading cause of disability worldwide.
In 2021, 1.7 million Americans attempted suicide. We lost 48,183.
MHealth Interventional Psychiatry Program

Ketamine

Treatment Resistant Depression

Advanced Pharmacotherapy

Behavioral Activation

TMS

ECT

Transcranial Magnetic Stimulation
Induction

Michael Faraday (1791–1867) - Qualitative

James Clerk Maxwell (1831–1879) - Equation

\[ \nabla \times \mathbf{E} = -\frac{d\mathbf{B}}{dt} \]

"Faraday EMF experiment"

Induction in Action

COIL CURRENT AND MAGNETIC FIELD

Magnetic Field
1-3 Tesla Peak

Stimulating Coil Winding
Typically 5-20 Copper Turns

Discharge Current
~8000 Amps Peak

brain diagram
Patterned Repetitive TMS (rTMS)

- **1 Train Multiple Stimuli**
- **Intertrain Interval**

- **High Frequency = > 1 Hz Train – Stimulatory**
- **Low Frequency = < 1 Hz Train – Inhibitory**

Stimulation parameters available for rTMS to TBS

1. **1 Hz rTMS**
2. **10 Hz rTMS**
3. **18 Hz rTMS**
4. **cTBS**
5. **iTBS**
## Treatment Timeline

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Referral by Primary Provider to Psychiatrist on TMS team</th>
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<tbody>
<tr>
<td>Step 2</td>
<td>Evaluation by TMS-privileged Psychiatrist</td>
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<table>
<thead>
<tr>
<th>Step 3</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
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<tbody>
<tr>
<td>Week 1</td>
<td>MTM + Tx</td>
<td>Tx</td>
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<tr>
<td>Week 2</td>
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<td>Week 4</td>
<td>MT + Tx</td>
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<tr>
<td>Week 5</td>
<td>MT + Tx</td>
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<td>Week 6</td>
<td>MT + Tx</td>
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<td>Week 7</td>
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<td>Week 8</td>
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*MTM = Motor Threshold Mapping (90 min appt), MT = Motor Threshold Determination (60 min appt), Tx = Treatment (10-60 min appt)*

**Ketamine**
A single ketamine infusion rapidly improves symptoms of depression. \((N = 18)\)

Repeated infusions increase response & durability. \((N = 24)\)
A greater proportion of patients who received ketamine were without suicidal ideation compared to placebo.


Titration to maintenance

Ketamine IV 0.5-1.25 mg/kg IBW x 40 min.

Acute
2-3 weeks
Total doses: 6-9

Continuation
1 month
Total doses: 4

Optimization + Maintenance
Titration in 1-2 month intervals
Total doses: indefinite
Eligibility (MDD)

- Individuals without medical exclusions by history
  - (e.g. kidney failure, heart failure, arrhythmia, glaucoma, liver disease)
- Routine lab work-up (pre-op PE) + negative UPT (women)
- No history of substance use disorder within the past 6 months
  - (strong recommendation to exhaust alternative treatment modalities in individuals with a history of opioid use disorder or polysubstance use disorder)
- *Failure of a neuromodulation treatment modality*
- Benzodiazepine taper prior to initiation of ketamine (if taking)

Eligibility for Maintenance

- Must meet response criteria on an outcome measure by the end of the acute period (after 6 to 9 infusions)
  - MADRS, PHQ-9, IDS-SR
- Must maintain response for a minimum of 1 week
  - Discussion of concerns for tachyphylaxis with weekly dosing
  - Encourage engagement in psychotherapy
  - Encourage use of Behavioral Activation strategies to maximize time between infusions
  - Strong recommendation for DBT if managing chronic SI
Electroconvulsive Therapy (ECT)
Electrode placement

![Bilateral](image1)
![Right unilateral](image2)
![Bifrontal](image3)

Acute course of ECT

- Index course 6 - 8 Txs
- 2 - 5 Txs per week
- Tx until improvement plateaus
- Continuation/Maintenance ECT
- Prophylactic medication
Indications for ECT

- Treatment-refractory conditions
- Severe or life-threatening psychiatric illness
- Most often used for the treatment of medication-resistant depression (MDD)

Vagus Nerve Stimulation (VNS)
Brain Stimulation Tools

- Electroconvulsive therapy (ECT)
- Magnetic seizure therapy (MST)
- Focal electrically-administered seizure therapy (FEAST)
- Auricular Vagus Nerve Stimulation (taVNS)
- Trigeminal Nerve Stimulation
- Transcranial Direct Current Stimulation (tDCS)
- Transcranial magnetic stimulation (TMS)
- Focus ultrasound (FUS)
- Focal electrically-administered therapy (FEAT)
  - **Convulsive**
  - **Sub-Convulsive**
  - **Cervical Vagus Nerve Stimulation (VNS)**
  - Deep brain stimulation (DBS)
  - Responsive Neurostimulation (RNS)
  - Prefrontal cortical stimulation (PCS)

**(invasive) Cervical VNS**
RCT Design (D-02; 2001)

Long-Term Analyses Demonstrate Response Rates Increase Over Time During Adjunctive VNS Therapy
FDA Approval
1998-2005

Controversy and CMS
2007 – 2018
(CMS determined VNS for TRD non-covered)

A 5-Year Observational Study of Patients With Treatment-Resistant Depression Treated With Vagus Nerve Stimulation or Treatment as Usual: Comparison of Response, Remission, and Suicidality

Scott T. Aaronson, M.D., Peter Sears, C.C.R.P., Francis Ruvuna, Ph.D., Mark Bunker, Pharm.D., Charles R. Conway, M.D., Darin D. Dougherty, M.D., Frederick W. Reimherr, M.D., Thomas L. Schwartz, M.D., John M. Zajecka, M.D.
Behavioral Activation

Vicious Cycle of Depression

Positive Cycle of Activity
Texas Medication Algorithm for nonpsychotic MDD

UMN Interventional Psychiatry Treatment Algorithm

Monotherapy
- SSRI
  - ↓
  - SNRI
  - ↓
  - TCA
  - ↓
  - MAOI

TMS
- BA
  - F8 rTMS
  - H1 rTMS
  - TBS

Ketamine
- IN
- IM
- IV

VNS

ECT

Clinic Renovation 2022-2023

- 17 patient exam rooms
- 3 team workspaces
- 18 touchdown spaces
- 7 individual work alcoves
- 2 two-person shared work spaces
- 3 TMS treatment rooms
- Infusion space with 3 infusion bays
- Phlebotomy space
- 2 acupuncture treatment rooms
- Lactation room
- 2 CMA stations with adjacent vitals stations
Renovation Blueprint

Becky's Story