

Overview: ECT and rTMS

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Goals:

- To understand the procedures, practice, and current theories of the mechanisms of both ECT and rTMS.
- To be familiar with the indicated and currently recognized uses of each modality, as well as the potentials for their use in the future.
- To be able to differentiate the appropriate application of each treatment modality, with a focus on patient selection for optimal outcomes.



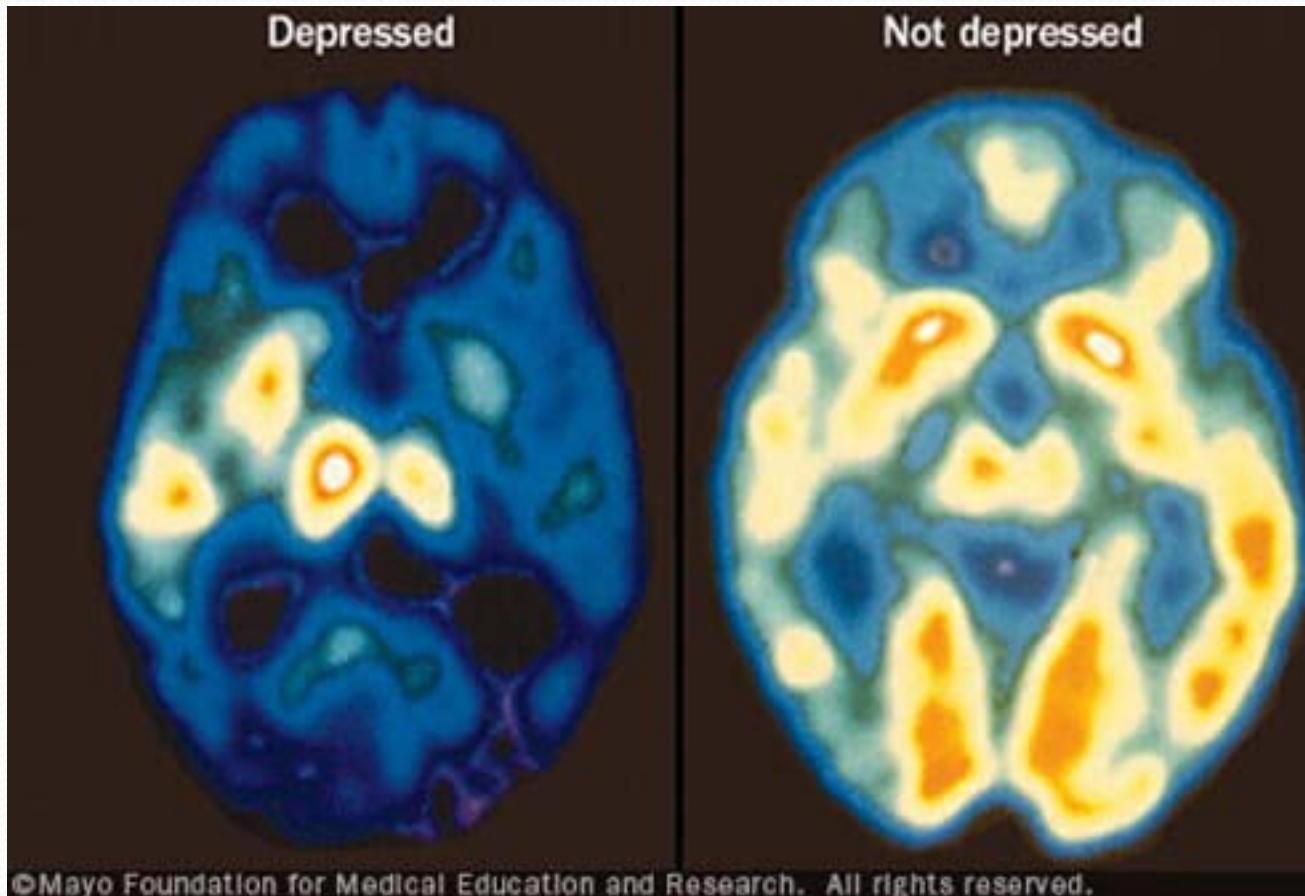
Disclosure

- I have no financial relationships with any commercial interest related to this presentation to disclose.
- I will be discussing unapproved uses of commercial products, or investigational use of a products not yet approved for these purposes, during my presentation at this educational activity.

Outline

- Impacts of untreated depression for context
- ECT (Electroconvulsive Therapy)
 - History
 - Modern procedure
 - Indications/predictive factors
 - Efficacy
 - Side effects/drawbacks
- rTMS (repetitive Transcranial Magnetic Stimulation)
 - Also future applications
- Discussion/Q&A

Depression: Impact



ECT: History

- **1927:** Sakel : Insulin Shock Therapy: Insulin induced coma with occasionally hypoglycemic convulsions : First biologic treatment for schizophrenia
- **1930's:** Von Meduna-hungarian psychiatrist discovered therapeutic value of seizures using camphor and Metrazol
- **1938:** Cerletti and Bini italian psychiatrists induced seizures utilizing electrical stimulus: no anesthetic or muscle relaxant
- **1940's:** first used in the US
- **1950's:** anesthesia was first introduced for ECT
- **1950-70:** significant overuse of ECT for treatment of conditions like character disorders, psoriasis, enuresis, ulcers
- **1970's:** widespread use of antidepressant and antipsychotic medications decreased the use of ECT
- **1990's:** improvements and modifications improved safety and reduced side effects: resurgence of ECT



ECT: Portrayals and Controversy

- ECT in literature and, more commonly, in film shows it as a negative and cruel treatment, and leaves the mistaken impression of a brutal, harmful, and abusive maneuver with no therapeutic benefit
- Commonly thought of images of ECT come from *The Snake Pit* (1948), *One Flew Over the Cuckoo's Nest* (1975), *Requiem for a Dream* (2000), *Girl Interrupted* (1999)
- A lightning rod for the anti-psychiatry movement
- Far from accurate portrayals of the modern practice of ECT



ECT: Modern Basics

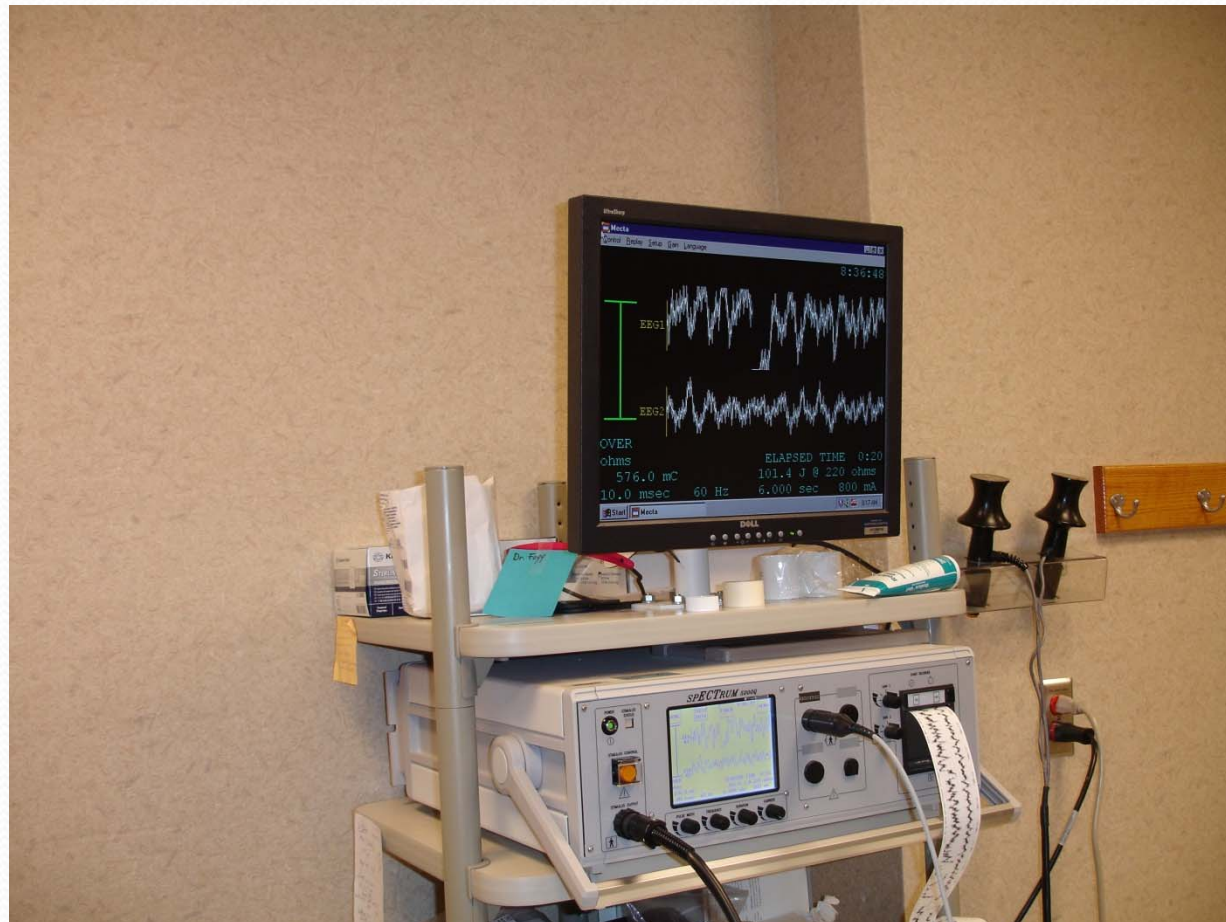
- Anesthesiologist
 - Propofol or brexital
 - Succinylcholine or rocuronium
- Pulses instead of sine-wave delivery of energy
- Regular, Brief, Ultra-brief delivery
- Right unilateral, bilateral, bifrontal placement



ECT: What happens

- Procedure lasts 5-15 minutes
- Recovery period 30 min
- Treatments 3 times a week, with index course of 6-20 treatments
- Continuation/Maintenance treatment option

ECT Devices



ECT Devices





ECT: How it works

- We're still not really sure
- But...

ECT: How it works (Theories)

- Von Meduna (1934)- Autopsies of patients w/seizure disorders and of patients w/Schizophrenia: Difference in Glial cell proliferation
- Neurotransmitter levels all increase after seizure
- Enhanced dopaminergic and serotonergic transmission, increased noradrenergic function
- During seizure- PET studies show an increase in BBB permeability and in cerebral blood flow and metabolism.
- After seizure, blood flow and metabolism is decreased especially in the frontal lobes. Research shows this correlated w/ response.
- Reduction of cholinergic sensitivity-reduction of brain Ach levels and increase of Choline acetyltransferase and acetylcholinesterase
- Recruitment of GABA; downstream recruitment of glutamate
- Cortisol burn-out



ECT: Primary Indications

- Major Depression
- Catatonia
- Schizophrenia
- Schizoaffective Disorder
- Mania



ECT: Other Indications

- Life threatening delirium
- OCD- no controlled studies
- Autistic self-injury
- Pseudo-dementia
- Parkinson's Disease- presence of off-on phenomenon predictive of positive response (treats rigidity)
- NMS
- Intractable epilepsy/status epilepticus



ECT: Positive Predictors

- Acute episode
- Prior good response
- Low energy
- Weight loss
- Delusions
- Poor concentration
- Acute catatonia



ECT: Negative Predictors

- Chronicity
- Poor relationships
- Axis II Disorder
- Substance Abuse
- Poor response to ECT in the past



ECT: Use as first-line

- Consider primary use of ECT with the following:
 - Need for rapid definitive intervention
 - Medically ill, risk of inanition including extreme slowing with poor intake and significant weight loss
 - Psychotic depression, catatonia, manic delirium
 - Risk of suicide
 - Treatment history – previous ECT response
 - Pregnancy
 - Patient preference
 - Lack of clinical response to multiple med trials
 - Intolerable medication side effects



ECT: Contraindications

- There is only ONE suggested absolute medical contraindication to ECT: Cochlear implant
- Risk/benefit analysis is performed by psychiatrist, medical doctor and ECT consultant



ECT: When to use caution

- Cardiovascular:
 - Pacemakers, AICD
 - Anticoagulation Therapy
 - Recent MI
 - Unstable angina
 - Uncompensated CHF
 - Severe valve disease
 - Aneurysms
- Central Nervous System:
 - Increased ICP
 - Intracerebral mass
 - Recent CVA
 - Pre-existing neurological disorders that predispose to delirium (MS, MG, basal ganglia dz, etc.)
- Severe burns or muscle injury (possible hyperkalemia)
- Pulmonary impairment
- High anesthesia risk (ASA level 4 or 5)



ECT: Efficacy/Benefits

- Depressive Episode: naturally have 46% spontaneous remission by 31 mo, 30-50% response rate (much lower remission rate) to medications in 4-8weeks, ~80-85% respond to ECT within 6-15 sessions (2-5 weeks) with a high percentage of those reaching remission (~60%)
- Catatonia: ~90% response rate to ECT, rapid
- Schizophrenia: ~75% have symptom improvement, chronic treatment sometimes needed to maintain improvement



ECT: Side Effects/Drawbacks

- Headache, muscle aches
- Nausea (from anesthesia)
- Brief confusion
- Memory impairment
 - Retrograde—for events nearest time of treatment patients may have gaps in their memories
 - Anterograde amnesia-rapid forgetting of newly learned information-until this resolves patient needs to be restricted from work, activities, driving etc
- No driving (or working some jobs) during treatment and for a short period after course ends
- Some medications are incompatible with treatment and need to be stopped before getting ECT



ECT: Safety

- Over 100,000 people in the US receive ECT every year
- Mortality is lower than for normal childbirth or any surgical procedure
- 1 per 80,000 treatments vs 18.5 for every 100,000 births
- Lower mortality rates in depressed patients receiving ECT than alternative treatment
- Most patients ultimately prefer ECT over routine dental care

TMS: History

- TMS, was first developed to use as a brain mapping tool, to measure cortical excitability, as a probe of neuronal networks, and as a modulator of brain function.
- Investigated for treating migraines
- In 1995, first documented human case report of rTMS in MDD





rTMS Basics

- Based on MRI technology
- FDA approved for the treatment of Depression in November 2008, in specific circumstances
- Non-invasive
- No anesthesia or sedation
- Approximately 35-45 minute daily (5x week) procedure
- 4-6 week treatment course
- No restrictions on driving
- Compatible with *most* medication regimens



TMS: What happens

- First treatment takes longer, have to find how much energy to use
- Treatment sessions: ~45 minutes daily
- Treatment course:
 - 5x/week for 4 to 6 weeks
 - Then taper over ~3 weeks











TMS: How it Works

- Based on Faraday's Law
- The electric coil creates a magnetic field that can penetrate through the skull into the brain 2-3 cm. directly under the coil
- This causes very small electrical currents in the brain that activate cells by causing depolarization and subsequent trans-synaptic changes
- When placed over the left dorsolateral prefrontal cortex (DLPFC), can affect cells that interact with the limbic system in a way that can stimulate activity that decreases depressive symptoms



TMS: Indications

- Its use is approved for the treatment of depression that has one failed adequate trial of an antidepressant in the current episode of depression, for treatment-resistant depression, or for patients unable to tolerate the side effects of medications.

American Psychiatric Association Treatment Guidelines for Depression

First Line Treatment Attempts

NEXT TRIAL

4-6 Weeks
TMS
Non-Invasive
Non-Systemic

Single Antidepressant Medication Maintenance

NEXT TRIAL

Antidepressant Switch
■ Non MAOI Class
■ MAOIs / TCAs

NEXT TRIAL

Augmentation Strategies

NEXT TRIAL

Atypical Antipsychotic Augmentation

On-going **Multiple** Antidepressant Medication Maintenance

2 Months

4 Months

6 Months+



TMS: Contraindications

- It's a mini-MRI, so... metal near the coil
- And that's it



TMS: Efficacy

- ~60% response rate (higher for some types of depression) and ~40% remission rate
- rTMS therapy shows improvements in standard measures of functional status and quality of life
- When rTMS is compared to current standard of care using complex combination antidepressant medications
 - TMS results in decreased number of days lost due to illness, and increased work productivity,
 - TMS results in a net cost savings relative to current pharmaceutical standard of care



TMS: Side Effects

- Mild headache
- Scalp tenderness at site
- During FDA approval process, had instance of a seizure, but post-approval no known reports
- Can trigger hypomania in susceptible patients if stimulants and caffeine are not avoided



TMS: Side Effects

- No systemic side effects such as weight gain, sexual dysfunction, nausea, dry mouth, or sedation
- No adverse effect on cognition
- No evidence of emergent suicidal ideation
- <5% of patients discontinued due to adverse events

rTMS future applications

- Psychiatric:
 - **Schizophrenia (negative symptoms and AH)**
 - *PTSD*
 - OCD
 - *Postpartum depression*
 - *Bipolar depression*
 - Mania
 - Suicidality
 - **Addiction and craving (specifically smoking cessation)**
 - **Bulemia nervosa**
 - ADHD

rTMS future applications

- Neurologic:
 - *Parkinson's disease*
 - ALS
 - MS
 - Post-stroke Aphasia, **Motor rehab**, *Neglect*, dysphagia
 - Writer's cramp
 - Chronic pain including trigeminal neuralgia, fibromyalgia, **neuropathic pain** in general, **CRPS**, and migraine
 - **Tinnitus**
 - *Epilepsy*
 - Essential tremor



Potential future treatments

- FEAST (Focally Electrically Administered Seizure Therapy)
- tDCS
- T-PEMF
- Trigeminal Nerve Stimulation
- MST (Magnetic Seizure Therapy)
- Low field magnetic stimulation
- Cranial electrical stimulation
- Invasive: VNS, DCS, DBS, Ablative neurosurgery



Selected resources:

- Rosenquist P, et al. Charting the Course of Electroconvulsive Therapy: Where Have We Been and Where Are We Headed?. *Psychiatr Ann.* 2016; 46: 647-651.
- Lefaucher, J-P, et al. Evidence Based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clinical Neurophysiology* 2014; 125: 2150-2206
- Book: Brain stimulation: Methodologies and Interventions (2015) John Wiley and Sons
- Book: Therapeutic rTMS in Neurology: Principles, Evidence, and Practice Recommendations (2016) Springer International Publishing