#CHAIR2017

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neuroscience CME

Master Class for Neuroscience Professional Development

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Effective Use of ECT: Treatment Decisions & Outcomes

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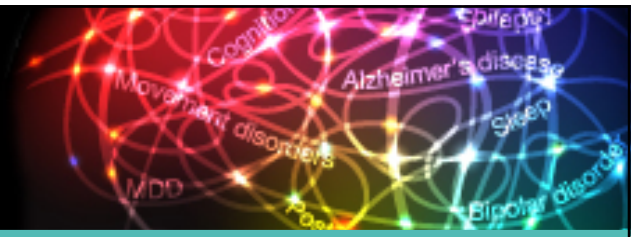
Disclosures

- ***Research/Grants:*** SAGE Therapeutics – Support for preclinical studies with oxysterols
- ***Consultant:*** Takeda Pharmaceuticals North America, Inc.
- ***Stockholder:*** SAGE Therapeutics
- ***Advisory Board:*** SAGE Therapeutics

Learning Objective 1

Incorporate the use of ECT to optimize clinical outcomes in individuals with treatment refractory depression

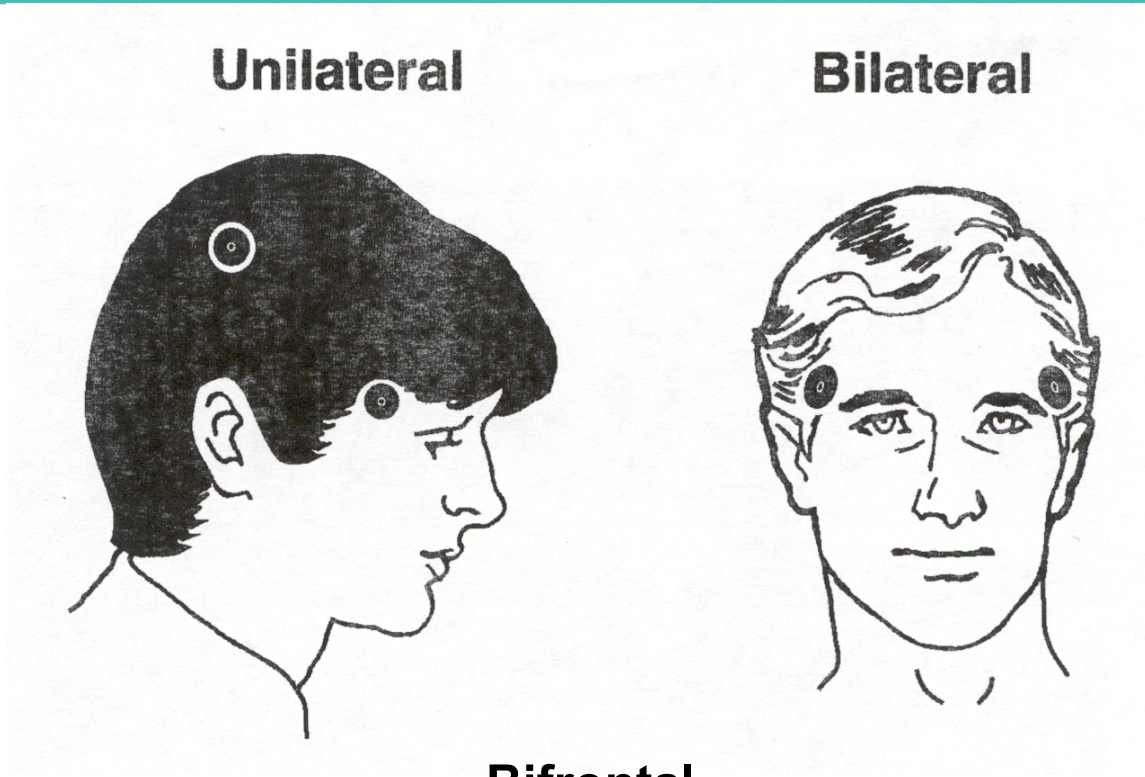
TRMD Proposed Definition



- STAR*D remission rates[1]
  - Remission rates at the four stages of treatment
    - 37% → 31% → 14% → 13%
  - Remission + maintenance x 1 year
    - 26% → 14% → 5% → 3%
- Two-stage TRMD definition[2]
  - Stage 1 TRMD: Failure of 2 adequate trials
  - Stage 2 TRMD: Failure of > 2 adequate trials

1. Rush AJ, et al. *Am J Psychiatry*. 2006;163(11):1905-1917; 2. Conway CR, et al. *JAMA Psychiatry*. 2017;74 (1):9-10.

Decision 1: Electrode Placement – Unilateral, Bilateral, or Bifrontal?



Bifrontal

Decision 2: Stimulus Waveform – How to Select Pulse Width & Frequency

Sine Wave (8.3 ms)

A

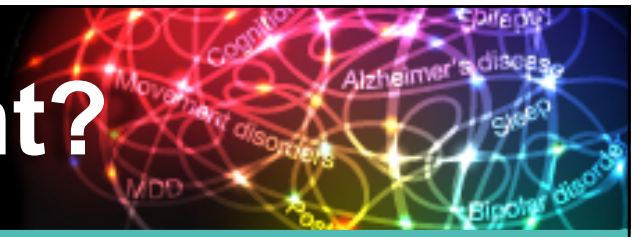
Brief Pulses (1.0-2.0 ms) – high frequency

B

Ultrabrief Pulses (<0.5 ms) – low frequency

C

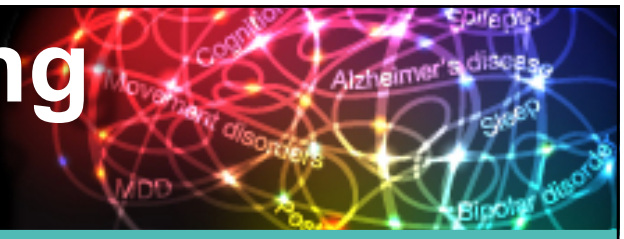
Why is Waveform Important?



- Long pulses & high frequencies are inefficient & contribute to cognitive impairment
- Shorter pulse widths give greater dynamic range for unilateral ECT with efficacy down to 0.3 ms pulses
  - Shorter pulses = fewer cognitive side effects
  - Responses to ultrabrief pulse right unilateral (RUL) ECT may be slower to develop and less complete
- Ultrabrief pulses (0.3 ms) may decrease responses to bilateral ECT

Tor PC, et al. *J Clin Psychiatry*. 2015;76(9):e1092-e10988. Sackeim HA, et al. *Brain Stimul*. 2008;1(2):71-83. Sackeim HA. *JAMA Psychiatry*. 2017;74(8):779-780; Cronholm B, et al. *J Nerv Ment Dis*. 1963;137:268-276.

Decision 3: Electrical Dosing To Titrate or Not to Titrate?



- Seizure thresholds vary ~10- to 20-fold
  - 25 mC to > 500 mC
- Without titration, it is unclear how to select electrical doses
  - Fixed doses do not account for individual variation
  - Excess stimulation = excess side effects
- Titration has some risk and often requires more than one stimulation
  - Risks are low based on our experience

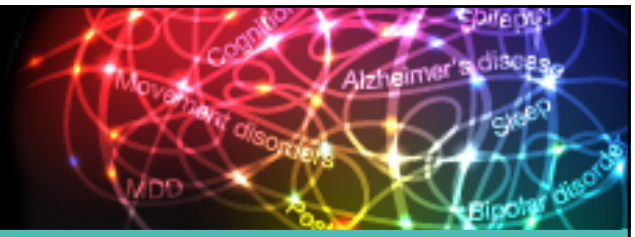
Isenberg KE, et al. *Ann Clin Psychiatry*. 2016;28(2):105-116.

Effective Use of ECT

- Optimize acute course by adjusting electrode placement, stimulus parameters, charge, number of treatments, and perhaps seizure length
  - Concurrent psychotropic medications may improve outcome but may add to memory problems
- Sequence of treatment
  - Right Unilateral (RUL) with ultrabrief pulses @ 6X threshold → Max charge RUL → 1.5 - 2.5X threshold bilateral with brief pulses → Max bilateral
  - ECT "Failure" = Failure of Max Charge Bilateral ECT
- Identify effective maintenance treatment

Sackeim HA, et al. *Arch Gen Psychiatry*. 2009;66(7):729-737.

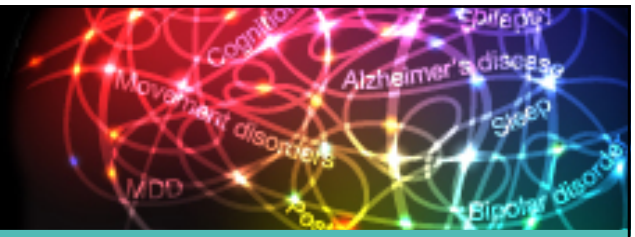
Decision 4: Maintenance



- Many ECT failures = failures of maintenance
  - Without successful maintenance, most patients will relapse in 6 weeks – 6 months
    - 84% (placebo); 60% (nortriptyline); 39% (lithium + nortriptyline)
- Maintenance strategies
  - Medications (different classes, combinations)
  - Evidence-based psychotherapies
  - Maintenance ECT
  - rTMS / VNS (?)

Sackeim HA, et al. *JAMA*. 2001;285(10):1299-307. Tew JD, et al. *Ann Clin Psychiatry*. 2007;19(1):1-4. Jelovac A, et al. *Neuropsychopharmacology.* 2013;38(12):2467-74. Kellner CH, et al. *Am J Psychiatry*. 2016; 173(11):1110-1118.

Call to Action



- ECT can be an effective form of treatment for TRMD, but you must think about the parameters of treatment and strategies to minimize side effects

Questions & Answers

Don’t forget to fill out your evaluations to collect your credit.