Transcranial Magnetic Stimulation (TMS)
TMS—the best intervention for treatment resistant major depressive disorder

• TMS is very safe and highly effective
• TMS is well tolerated
• The response to TMS is lasting
Repetitive Transcranial Magnetic Stimulation (rTMS)

- Results from over eight years of providing rTMS in private practice
- Indications and which patients respond the best
- Comparing FDA approved rTMS devices
- Future direction(s) for TMS
TMS is very safe and highly effective

• Mechanism of action
  • A changing magnetic field induces electrical current (Maxwell and Faraday)
  • MRI strength magnetic coil induces the magnetic energy that traverses the skull and into the cortex.
    • The time varying magnetic field induces current in the neurons of the superficial cortex that stimulates other neurons that are part of the circuit.

• Role of neuroplasticity
  • Effects continue after stimulation is finished
  • rTMS affects cortical excitability with high frequency pulses increasing cortical excitability and low frequency pulses decreasing cortical excitability.
Focus is on location

• Left prefrontal cortex
  • Window into the Limbic System and associated circuits
    • Amygdala, hippocampus, mammillary bodies, etc.
    • Stimulation continues downstream

• Other areas are focus for study
Efficacy of rTMS

• Over 20 years of research and development
• More than 30 published randomized controlled trials
• Over a dozen Meta-analyses
• Over 11 years of clinical experience in the community
• Primary focus has been antidepressant treatment
• O’ Reardon, et. al., 2007. Industry sponsored (N = 301)
  • Randomized to either active arm or sham
  • Patients failed four previous antidepressants
  • Outcomes measured at 4 and 6 weeks using MADRAS and Ham-D
  • Active treatment superior to sham at 4 and 6 weeks (p = 0.038)
    • Response defined as > 50 % improvement from baseline
    • Response was Two fold higher after 4 weeks and Three fold higher at 6 weeks
Large scale studies of rTMS (N > 100)

• George, et. al., 2010
  • Randomized to active or sham
  • Active arm showed superiority at week 3 (14 % vs 5 %)
  • Open label extension for patients not previously responding
    • 41 % responded and 30 % remitted
Meta-analysis

- Level 1 evidence since randomized controlled trials are included
- More than 12 meta-analyses have been conducted since 2000
  - Majority show statistical superiority of rTMS to sham treatments
  - Effect sizes ranged from those showing 50% to 80% improvement in depression scores
Clinical Effectiveness of rTMS

• Pooled data of nonresearch samples show robust results
  • Carpenter et al (2012) pooled data from 42 clinical practices (N = 307)
    • Average of 2.5 to 3.4 previously failed medication trials
    • 58 % responded and 37.1 % remitted
  • Connolly et al (2012) (N =100)
    • Single academic practice
    • Similar results 50.6 % responded and 24.7 % remitted
    • Included patients who had failed ECT
Comparison with Electroconvulsive Treatment (ECT)

- ECT has had over 75 years of use and modifications
- rTMS has been FDA approved for 11 years
- ECT has faster response rate
- rTMS is non-invasive
- rTMS can help improve cognition whereas memory problems are a hallmark side effect of ECT
- Most Head to Head studies have showed ECT as more effective
  - Limited by sample size and variations on the rTMS protocols used
rTMS is Well Tolerated

• Proven safe and effective for decades
  • Only contraindication is presence of magnetic sensitive metal above shoulders
  • In some cases implanted stimulators may be a problem

• Transient discomfort to area of treatment
  • Stimulation to superficial neurons
  • Intense 4 second train of pulses at 10 Hz
  • Discomfort is diminished over time
rTMS is Well Tolerated

- Patients with migraine may have headaches
- Seizures are rare
  - Meta analysis by Bae et al (2007) estimate risk is 1.4 %
  - Increased risk with alcohol use, sleep deprivation, or some medications
- Imaging studies show no structural changes after rTMS
- Human histological study (Gates et al 1992) showed no histopathological changes to temporal lobe of one patient
- Meta analysis (N = > 3000) (Machii et al 2006) showed no cognitive deterioration
TMS response is long lasting

- Durability studies show vast majority of patients have over a year of lasting response.
- My experience is that about 25% of patients need another treatment within two to three years.
- Majority of patients have not needed further rTMS and some have not had treatment for over 8 years.
- Subsequent treatments have better and longer lasting response than the previous treatment.
Results of over eight years experience providing TMS

• Well over 300 patients
• Results measured by PHQ-9 and Beck’s Depression Inventory
  • 67 % have had robust response (average improvement was 11 points)
  • Within the group of patients 43 % achieved remission
• Most patients note improvement by the end of treatment but some take a month or more to recognize the improvement
  • Role of neuroplasticity
• One patient using the Deep TMS system had a seizure
  • Sleep deprived and taking Bupropion
  • He elected to continue treatment and continued using different device and had no further seizures
Indications for TMS and which patients respond the best

• FDA cleared for Major Depressive Disorder
  • Moderate to severe and failed one adequate medication trial
• Insurance carriers require at least 4 antidepressant failures
• Patients with concomitant Personality Disorders may not respond as well
• Duration of current Depressive episode may or many not be a factor
Comparison of TMS Devices

• Physical effects dependent on shape of magnetic coil
  • Figure eight shape is most common
    • First one developed
    • Neuronetics NeuroStar and MagStim devices
  • H-shaped coil
    • Brainsway device
    • Deeper stimulation with stronger pulses
Comparison of TMS Devices

• Southern Maine TMS experience
  • Six years using either Neuronetics or Brainsway devices
    • Three years each device with 100 patients treated with each device
  • Same patient selection criteria
    • MDD, failed at least 4 antidepressants
  • Same treating technicians and protocols
Comparison of TMS Devices

• Results
  • Less deep stimulation had the best results
    • About 10% better results on PHQ-9
    • More patients could tolerate the treatment
  • Only patient to have a seizure in 8 years of treating patients was with the Deep TMS system
    • More patients dropped out of treatment with the Deep TMS treatment
    • Many moved to NeuroStar system and completed treatment
Future of TMS

• Early in the evolution of the treatment modality
  • Protocols for treating other conditions need development
    • Shapes of waveforms, pulse frequency, duration, location of treatment, etc.

• Conditions under investigation
  • Adolescent Major Depressive Disorder
  • Bipolar Depression
  • Obsessive Compulsive Disorder
  • Substance Dependence
    • Tobacco, Opioids, others
Future of TMS

• Conditions under investigation (continued)
  • PTSD
  • Parkinson’s Disease
  • ADHD
  • Cognitive Impairment
  • Tinnitus
  • Auditory Hallucinations
Conclusion

- rTMS is at least the best initial intervention for Treatment Resistant Depression (TRD)
- rTMS is safe and effective
- rTMS is well tolerated and has no cognitive side effects
- Future improvements to the current state of the technology are ongoing
- Many more conditions will be treated by this modality in the future
References

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