rTMS for Refractory Depression: Findings and Future

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What is Repetitive Transcranial Magnetic Stimulation?

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Patterned rTMS: Theta-Burst Stimulation

Continuous Theta-Burst Stimulation (cTBS)
50 Hz 5 Hz
Robust, durable inhibition >1 h after 600 pulses (~30 sec)

Intermittent Theta-Burst Stimulation (iTBS)
5 sec 2 sec
50 Hz 5 Hz
Robust, durable facilitation >1 h after 600 pulses (~30 sec)
Multiple Protocols, Multiple Targets

A Brief History of rTMS for Depression

1985 Barker et al.: first use of rTMS for motor cortex stimulation
1995 George et al.: report of rTMS improving mood in depression
1996 Pascual-Leone et al.: Lancet RCT of rTMS in depression
2002 Health Canada approval of rTMS for major depression
2007 O’Reardon et al.: Large USA multi-centre RCT of rTMS in MDD
2008 FDA approval of NeuroStar rTMS device for refractory MDE
2010 Holzheimer et al.: First report of ‘accelerated rTMS’ for MDE
2011 Several RCTs show increasing rTMS efficacy w refinements to Rx

A Typical Course of rTMS Treatment

15-30 daily sessions (Mon-Fri)
15-60 min / session
Outpatient setting

How well does it work?

“The results strongly suggest that focal rTMS to left prefrontal structures might obtain results similar to those of ECT, without requiring induction of seizures.”

Efficacy of rTMS: Meta-Analysis (2008)

Remitters
Responders
Nonresponders

Efficacy boosters for rTMS

1. Increase the stimulation strength
   80% -> 100% -> 120% RMT

2. Increase number of pulses / session
   800 -> 3000 -> >6000 pulses

3. Increase number of sessions / course
   5 -> 15 -> 30 - 40 sessions

4. Bilateral stimulation, new coil geometries
   R 1Hz, L 10 Hz, H-coil, angled coil

5. Improved targeting accuracy
   "5 cm rule" -> "6 cm rule" -> MRI-guided

Increasing efficacy of rTMS in recent trials

Adverse effects of rTMS

- >50% Transient scalp discomfort / headache
- 5% Pre-syncopal / syncope during initial session(s)
- 5% Fatigue post-session
- 1% Emergence of hypomania/mania in BD
- 1% Emergence of suicidal ideation (not acts)
- <1 in Induction of seizure during (not after) treatment
- 1000 (most antidepressants carry 0.1-0.5% seizure risk)

- NO cognitive/memory impairment (?? improvement)
- NO epilepsy as complication of treatment
- NO known long-term adverse effects

What are the risks?

Ideal candidates for rTMS

- Reside (or can stay) near rTMS clinic
- Primary diagnosis of mood disorder
  (unipolar OR bipolar are OK)
- Reliable, motivated, able to adhere to
  schedule of treatments dependably
- No previous failure of ECT or rTMS
- Life stressors at least somewhat optimized
- Have psychiatric follow-up available
  (medications, therapy, MBCT group)
A poor candidate for rTMS

Coming in from Ajax / Peterborough
Borderline PD & active polysubstance abuse, chronic low-grade depression
50% adherence to appointments
Tried ECT in 2005, no improvement
Living with ex-wife during divorce proceedings
"I need to find a new psychiatrist."

Relative Contraindications for rTMS:

Presence of metallic hardware near coil (cochlear implants, Internal Pulse Generators, medication pumps)

History of epilepsy (although low-freq is safe and used as Rx)
Brain lesion: vascular, traumatic, tumor, infection
Sleep deprivation, EtOH dependence / abuse
Implanted DBS electrodes, pregnancy, severe or recent heart disease

Medications lowering seizure threshold:
TCAs, CPZ, clonazepam, amphetamines, gancyclovir, ritonavir
Cocaine, MDMA, ketamine, PCP, w/d from EtOH, benzos, barbiturates
Mild risk with most SSRI s, SNRIs, FGAs and SGAs, Li, some abx


rTMS Sites in Toronto

Coming soon!

MINDCARE CENTRES

Before and After Treatment

No need to taper off / adjust meds before rTMS
Stable med regimen x 4 weeks before rTMS
Stable med regimen during rTMS
Stable meds x 4 weeks after rTMS is preferable
Duration of effect typically >6 months
Maintaining meds is advisable
Repeat treatments effective for relapse
MBCT / other therapy advised post-treatment

1-page referral for rTMS consult

416 603 5667

What’s on the horizon for rTMS in depression?
Sheline YI, Price JL, Yan J, Mintun MA. Resting-state functional MRI in depression unmasks increased connectivity between networks via the dorsal nexus.

What if we skip the DLPFC and target the DMPFC instead?

New coils can reach the DMPFC

Overall Efficacy of rTMS-dmPFC in MDD
Accelerated rTMS: 5 days, 5 sessions per day

Accelerated DLPFC - rTMS: 2 days to remission in 4/14

Holtzheimer PE 3rd, McDonald WM, Muth M, Kaley NE, Quinn S, Corso G, Epstein