TMS and Imaging

Joan A. Camprodon, MD MPH PhD
Chief, Division of Neuropsychiatry
Laboratory for Neuropsychiatry and Neuromodulation
Transcranial Magnetic Stimulation (TMS) clinical service
Massachusetts General Hospital, Harvard Medical School

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Neuropsychiatry: Disorders of Connectivity

Functional Neuroimaging Methods

Electrophysiologic: EEG/MEG

Metabolic and/or Vascular
- PET/SPECT
- fMRI
- NIRS

2 Axis of Resolution... or 3?

3rd Axis: Causality

Epiphenomenon!!
Brain Stimulation - Neuromodulation

- **Invasive**
  - Deep Brain Stimulation (DBS)
  - Vagal Nerve Stimulation (VNS)
  - Epidural Stimulation (ES)
- **Convulsive**
  - Electroconvulsive Therapy (ECT)
  - Magnetic Seizure Therapy (MST)
- **Noninvasive**
  - Transcranial Magnetic Stimulation (TMS)
  - Transcranial Direct Current Stimulation (tDCS)

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Neuromodulation: Need to know...

- The circuit(s)
- The target(s)
- Direction of modulation

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Transcranial Magnetic Stimulation

- 1831 Faraday's Electromagnetic Induction
- Anthony Barker 1984

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TMS Applications

- Measure brain activity
- Change brain activity

- Clinical: Diagnostics (neural system disorders) (pre-surgical mapping)
- Clinical: Therapeutics (circuit-based pathologies)
  - MDD
  - Acute Migraines
  - OCD
  - Smoking Cessation

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TMS limitations

- Where to stimulate?
- What does TMS do to the Brain?
  - Only behavioral measures? Beyond the black box approach.
### Functional Neuroimaging vs. TMS

<table>
<thead>
<tr>
<th>Neuroimaging</th>
<th>TMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlational (cannot establish causality)</td>
<td>Interventional (and thus causal)</td>
</tr>
<tr>
<td>Measures whole-brain activity</td>
<td>Measures behavioral outcomes</td>
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### Why Combine TMS and Neuroimaging?

- Plan, guide and document localization of TMS
- Develop circuit predictor biomarkers
- Measure neurobiological effects of TMS, beyond cognitive and behavioral outcomes

### TMS-fMRI vs PET/EEG

- Vs. TMS-PET
  - MRI: better spatio-temporal resolution
  - MRI: no need of radioligands (better potential for repeated measures)
  - PET: neurotransmitter dynamic or more complex biological process
- Vs. TMS-EEG
  - MRI: better spatial resolution
  - EEG: better temporal resolution
  - MRI: ability to measure subcortical structures with greater detail (anatomy)
  - EEG: diversity of physiological measures in frequency and time domain

### Anatomy: Therapeutic Targets

- OCD Target: DMPFC/pre-SMA
- MDD Target: DLPFC
- Migraine Target: Occipital pole
- Smoking Cessation: VLPFC/Insula

### Localization: Stereotactic Neuronavigation

- Task fMRI
- fNIRS
- fMRI
MDD Effectiveness: Naturalistic Studies

Carpenter et al. 2012
- 330 patient with MDD naïve to TMS
- Concurrent medications/therapy
- Response Rate: 41.5-58%
- Remission Rate: 20.5-37.1%

Group Level fcMRI Target: Prospective Trial

Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (TMB2D-C): a randomised non-inferiority trial

Individualized fcMRI-guided TMS

Individualized Targeting: Clinical Response

Why Consider TMS treatment for Depression?

fcMRI-guided Accelerated TBS for MDD

Stanford Neuromodulation Therapy (SNT): A Double-Blind Randomized Controlled Trial
Accelerated TBS for MDD

Stanford Neurmodulation Therapy (SNT): A Double-Blind Randomized Controlled Trial

- FDA cleared in 2022
- Interim Analysis: 30 patients (aim was 60)
- Cohen’s d > 0.8 → Study ended

Active:
- 62.0%, 70.9%, 62.4%, 57.8%, 52.5%

Sham:
- 14.3%, 20.6%, 10.4%, 10.9%, 11.1%

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Neuroimaging DURING TMS

Neuroimaging BEFORE TMS

Neuroimaging AFTER TMS

Individualized Targeting: Clinical Response

HAMD 17

Responders

Non-Responders

Remitters

- Responders: 50% (10/20)
- Non-Responders: 50% (10/20)
- Remitters: 50% (10/20)

Failed medications in current episode: 7.06 (range 5 - 12)

Node to Node effects

Target of Stimulation with SCC

Baseline Connectivity

Change in Connectivity

Target of Stimulation
**Node to Network Effects**

- **Visual**
- **Somatomotor**
- **Dorsal Attention**
- **Frontoparietal**
- **Limbic**

**SCC with Default Mode Network**

**Summary**

- **Clinical Outcomes**
  - Individualized fcMRI-guided TMS leads to 50% response and remissions rate in highly treatment-resistant patients.
  - Much improved remission rate than standard TMS: seems to justify individualized vs. group target.
  - All or nothing distribution: what are we missing in ½ patients?

- **Node to node (DLPFC to SGC) dynamics**
  - Weak baseline connectivity predicts greater response
  - Clinical response explained by strengthening of the anticorrelation

- **Node to Network dynamics**
  - Connectivity from the DLPFC target does not explain or predict clinical response
  - SGC connectivity to DMN predicts and explains response (distant effects)
  - Weak baseline positive correlations predict good response
  - Response is associated with strengthening of positive connectivity
  - Distal effects more important than local changes in the DLPFC target (network mechanism)