rTMS 360°

National Conference & Hands-On Workshop

Organised by

Department Of Psychiatry &
Medical Education Unit

Supported by

Neuromodulation Society of India (NSI)

August 14, 2025

Sree Balaji Medical College & Hospital, Chennai

Preface

It is with great pride that we present the **rTMS 360° Handbook**, created in conjunction with the **National Conference & Hands-On Workshop on Repetitive Transcranial Magnetic Stimulation (rTMS)**, organized by the **Department of Psychiatry & Medical Education Unit, Sree Balaji Medical College & Hospital**, with the support of the **Neuromodulation Society of India**.

This handbook has been designed as both a scientific reference and a practical guide for clinicians, researchers, and trainees interested in neuromodulation. It brings together the latest consensus guidelines, recent technological advances in coil design and targeting methods, and clear, step-by-step workflows for safe, effective, and reproducible rTMS delivery.

We acknowledge with appreciation the contributions of our **distinguished faculty speakers**:

Dr. Ragul Ganesh R., Assistant Professor, JIPMER, Puducherry
Dr. Shubham Narnoli, Consultant Psychiatrist, MindfulTMS Neurocare, New Delhi
Dr. Rohit Verma, Professor, AIIMS, New Delhi
Dr. S.P. Murugappan, Senior Consultant Psychiatrist, Ultimate Brain Clinic, Chennai

Our thanks also go to our **chairpersons**, who facilitated engaging and insightful discussions:

Dr. Sabari Sridhar O.T., HOD Psychiatry, Sri Ramachandra Medical College & Research Institute
Dr. Rajkumar R., Retired Professor & HOD, Psychiatry, SBMCH
Dr. Suresh Kumar M., Senior Consultant Psychiatrist

Organizing Committee,

Dr. Priya Sivashankar., Professor and HOD of Psychiatry
Dr. Gopinath S., Associate Professor
Dr. Farhana M., Assistant Professor
Dr. Srinivas Rajkumar T., Assistant Professor
Dr. Monisha S., Assistant Professor
Dr. Rammya K., Senior Resident
Dr. Annie Sheena, Senior Resident

Note from the Editor

This book is designed as a *living resource*. The content will be continuously updated to reflect emerging evidence, new protocols, and evolving safety recommendations. We recognise that no single edition can remain definitive in a rapidly progressing field like neuromodulation.

Your feedback is essential to ensure this work remains relevant, accurate, and practical. If you have suggestions, corrections, or comments, please email them to **srinivasaiims@gmail.com**.

Together, we can keep this handbook at the forefront of clinical and research excellence in rTMS.

rTMS 360° Handbook

Index

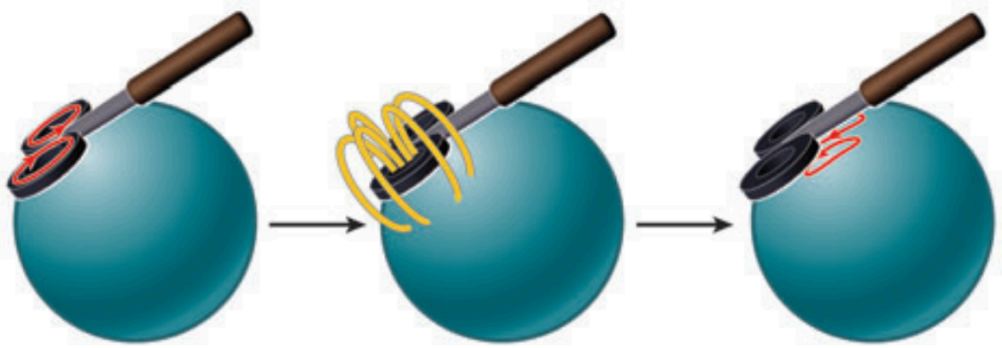
Chapter 1

Introduction

Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation technique that uses rapidly alternating magnetic fields to induce small electrical currents in targeted cortical areas. These currents can either enhance or suppress neuronal activity, making TMS a powerful tool for exploring brain function and modifying abnormal neural patterns seen in various neuropsychiatric disorders.

When delivered repetitively, as in Repetitive Transcranial Magnetic Stimulation (rTMS), the stimulation produces longer-lasting changes in cortical excitability. The therapeutic rationale is grounded in *Faraday's Principle of Electromagnetic Induction*:

Electric Current in Coil → Magnetic Field → Induced Current in Brain Tissue



rTMS generates currents within the brain using externally applied magnetic fields—without placing electrodes directly on or inside the brain—it is often described as an "electrodeless" form of electrical brain stimulation. This approach not only avoids the discomfort associated with direct electrical contact but also enhances safety by eliminating the risk of tissue damage from implanted hardware.

By modulating dysfunctional brain networks—without the need for surgical intervention or implanted electrodes—rTMS offers a safe, well-tolerated, and evidence-based intervention for conditions such as depression, obsessive-compulsive disorder, neuropathic pain, and post-stroke rehabilitation. In clinical practice, rTMS is increasingly valued for its ability to target brain regions with precision, adapt stimulation parameters to individual needs, and achieve sustained symptom relief through non-invasive means.

Historical Overview

- 1985 – Anthony Barker et al. first described TMS as a single-pulse cortical stimulator.
- 1990s – rTMS adopted in clinical settings, primarily in research contexts.
- 2008 onwards – Multiple FDA clearances for various devices and protocols (Major Depressive Disorder, OCD, migraine prevention, smoking cessation).
- Recent trends – Expansion into accelerated and patterned protocols (e.g., Theta Burst Stimulation, Quadri-Pulse Stimulation), neuronavigation-guided targeting, and applications across psychiatry and neurology.

Rationale for rTMS in Psychiatry

Despite advances in pharmacotherapy and psychotherapy, 20–60% of patients with psychiatric disorders remain non-responsive to first-line treatments. Factors such as adverse effects, stigma, and limited psychotherapy access contribute to this “pseudo-resistance.” rTMS offers an evidence-based, well-tolerated alternative or augmentation strategy in these case

Mechanism of Action

- Electromagnetic induction: Based on Faraday’s principle—current in a coil generates a magnetic field, inducing secondary currents in brain tissue.
- Neurophysiological: Modulates cortical excitability through long-term potentiation (LTP) or depression (LTD)–like effects.
- Neurochemical: Alters glutamatergic, GABAergic, dopaminergic, and serotonergic transmission.
- Network-level: Resets dysfunctional connectivity patterns in large-scale brain networks (e.g., Default Mode Network, Salience Network).

Current Applications

FDA- and CE-approved indications include:

- Major Depressive Disorder (including treatment-resistant depression)
- Obsessive-Compulsive Disorder
- Smoking cessation
- Migraine prevention

Investigational and off-label uses:

- Post-stroke depression and motor recovery
- Generalized anxiety disorder
- PTSD
- Schizophrenia (negative symptoms, auditory hallucinations)
- Substance use disorders
- Chronic pain syndromes
- Autism spectrum disorder and other neurodevelopmental conditions

Why This Handbook?

This 2025 edition integrates:

- Latest IPS 2023 Clinical Practice Guidelines and international consensus safety recommendations.
- Advances in coil technology, stimulation paradigms, and targeting methods.
- Evidence synthesis from recent meta-analyses across psychiatric and neurological disorders.
- Practical, step-by-step guidance for clinicians, from patient selection to protocol optimization.

Chapter 2

Basic Principles of rTMS

1. Physics and Mechanism

Repetitive Transcranial Magnetic Stimulation (rTMS) works on Faraday's Principle of Electromagnetic Induction:

> A rapidly changing electric current in a coil → generates a magnetic field → induces an electrical current in underlying brain tissue.

Because no direct contact electrodes are placed on the brain, rTMS is termed *electrodeless electrical stimulation*.

- Magnetic field strength: Typically up to 2 Tesla at the coil surface.
- Depth of penetration: Around 2–3 cm into the cortex for figure-of-eight coils, deeper for H-coils.
- Neurophysiological effect: Depending on frequency and pattern, stimulation can increase or decrease cortical excitability, mimicking LTP or LTD mechanisms.

2. Pulse Types and Waveforms

- Monophasic: Current flows in a single direction, producing more focal stimulation; useful in diagnostic single-pulse TMS.
- Biphasic/Polyphasic: Current reverses direction; commonly used in therapeutic rTMS for efficiency and coil cooling.
- Patterned protocols:
    - Theta Burst Stimulation (TBS): Short bursts of high-frequency pulses (50 Hz) repeated at theta rhythm (5 Hz).
        - iTBS (intermittent): Facilitatory effect.
        - cTBS (continuous): Inhibitory effect.
        - imTBS (intermediate): Under investigation.
    - Quadri-Pulse Stimulation (QPS): Four pulses in rapid succession at variable inter-pulse intervals.

3. Stimulation Strength and Motor Threshold

Stimulation intensity is expressed as a percentage of the individual's resting motor threshold (RMT):

- RMT definition (IPS, 2023): *Minimum intensity that produces a visible muscle twitch (usually in the contralateral abductor pollicis brevis) in ≥5 out of 10 trials*.

- Determined before treatment; re-assess weekly or when medications change, alcohol/substance use occurs, or if patient reports new scalp pain/headache.

4. Stimulation Frequencies and Effects

Frequency	Typical Effect	Example Clinical Use
≤1 Hz (Low freq.)	Reduces cortical excitability (LTD)	Anxiety, auditory hallucinations
>5–20 Hz (High freq.)	Increases cortical excitability (LTP)	Depression, negative symptoms in schizophrenia
Theta Burst (iTBS)	Facilitatory effect, shorter session	Depression
Theta Burst (cTBS)	Inhibitory effect	Tinnitus, craving

5. Coil Types and Target Depth

- Figure-of-Eight (F8) coil: Most common; focal stimulation of superficial cortex.

- Round coil: Less focal, rarely used for therapeutic protocols.

- Double-cone coil: Deeper penetration, useful for leg motor cortex and SMA.

- H-Coil: Deep TMS; stimulates bilateral and deeper cortical/subcortical regions.

- Cool-B65 & air/liquid-cooled coils: Allow higher duty cycles and prolonged sessions without overheating.

6. Target Localisation Methods

- Scalp-based:

    - *5 cm rule*: From motor hotspot, 5 cm anterior along a parasagittal line.

    - *International 10–20 EEG system*: Cost-effective, standardised scalp mapping.

- Image-guided neuronavigation:
    - MRI-based targeting (structural, functional, or connectivity-guided).
    - Improves reproducibility and precision, especially in research and TRD.

7. Stimulation Paradigms

- Single-pulse TMS: Diagnostic use in neurophysiology and corticospinal excitability measurement.
- Paired-pulse TMS: Research tool for assessing cortical inhibition/facilitation.
- Repetitive TMS (rTMS): Therapeutic use — trains of pulses designed to produce sustained neuroplastic changes.
- Accelerated protocols: Multiple sessions/day; promising in TRD but require further large-scale validation (e.g., SAINT protocol).

8. Influencing Factors

Efficacy and tolerability depend on:

- Stimulation site and coil orientation.
- Frequency and pattern of stimulation.
- Number of pulses per session and total treatment sessions.
- Patient-specific factors — age, illness duration, baseline cortical excitability.

Parts of the rTMS System

An rTMS setup consists of core components and supportive accessories that together enable safe, precise, and reproducible stimulation.

1. Main Unit (Stimulator)

- Charging System: Generates the high currents required for stimulation (up to 8,000 A within a few hundred milliseconds).
- Energy Storage Capacitors: High-voltage (up to ~7.5 kV) capacitors store and rapidly discharge energy for each pulse.
- Energy Recovery Circuitry: Recycles unused energy after each pulse, improving efficiency.
- Switching Device (Thyristor/IGBT): Connects capacitors to the coil, discharging up to 500 J in under 100 ms.
- Pulse-shaping Circuitry: Configures output waveform (monophasic, biphasic, polyphasic).

2. Stimulating Coil

Different coil types influence depth, focality, and clinical effect:

- Figure-of-Eight (F8): Most common; focal stimulation to ~2–3 cm depth.
- Round Coil: Broader field; less focal.
- Double-Cone Coil: Deeper cortical targets (e.g., SMA, leg motor cortex).
- H-Coil: Deep TMS; reaches bilateral and subcortical targets.
- Cool-B65 / Air- or Liquid-cooled Coils: Prevent overheating in high-frequency or long sessions.

IPS 2023 Recommendation: For research, have at least two F8 coils, plus placebo coil if sham studies are planned.

3. Cooling System

- Air Cooling: Fans dissipate heat from the coil.
- Liquid Cooling: Circulates coolant for heavy-duty, high-frequency, or deep TMS protocols.
- Temperature Sensors: Automatic shutdown if overheating detected.

4. Coil Holder and Positioning Systems

- Gooseneck / Articulating Arms: Manual adjustment for comfort and accuracy.
- Motorised or Robotic Positioning Systems: Allow automated repositioning and consistent targeting (increasingly used with neuronavigation).

5. Control and Targeting Interface

- Standard Controls: Touchscreen or hardware interface for parameter programming (frequency, train duration, inter-train interval, pulse count).
- Neuronavigation Systems:
    - Integrate MRI data to locate and track the stimulation target in real time.
    - Provide visual feedback to maintain coil position and angle throughout the session.

6. Patient Interface

- Treatment Chair: Comfortable recliner with adjustable headrest; back height must allow coil placement.
- Head Stabilisation: Cushions, straps, or chin rests to reduce movement.
- Ear Protection: Disposable earplugs providing ≥30 dB noise reduction for both patient and operator.

7. Electromyography (EMG) System *(Optional but recommended for precise motor threshold determination)*

- Surface electrodes record motor-evoked potentials (MEPs) from target muscles.
- Helps objectively define stimulation intensity and monitor corticospinal excitability.

8. Power Supply & Backup

- UPS / Stabiliser: Protects equipment from voltage fluctuations and ensures safe shutdown in power failure.
- Surge Protectors: Prevents damage from electrical spikes.

9. Safety & Emergency Equipment

- Anticonvulsant medication (e.g., IV benzodiazepine) ready for seizure management.
- First aid kit and resuscitation equipment.
- Immediate availability of trained medical staff.

IPS 2023 Minimum Technical Specs (for therapeutic and research use)

Component	Specification
Stimulator	≥50 Hz capacity with burst mode for TBS (20 Hz basic without burst mode acceptable for limited clinical use)
Coils	Air or liquid-cooled Figure-of-Eight (min. 2); placebo coil for research
Accessories	Trolley, coil holder, treatment chair
Desirable Add-ons	USFDA/CE/ISO certification, integrated EMG, deep TMS coils, upgradable neuronavigation

Chapter 4 :

Stimulation Paradigms in rTMS

The therapeutic effect of rTMS depends on frequency, pattern, site of stimulation, and total dose (pulses/session × number of sessions).

Different paradigms can either increase or decrease cortical excitability.

1. Single-Pulse TMS

Definition: A single magnetic pulse applied to a cortical site.
Purpose: Diagnostic and research use — measuring motor evoked potentials (MEPs), conduction times, cortical excitability.
Clinical Role: Baseline mapping and motor threshold determination.

2. Paired-Pulse TMS

Definition: Two pulses in close succession — the first ("conditioning") modulates the effect of the second ("test").
Inter-pulse intervals:
Short intervals (1–5 ms) → inhibition.
Long intervals (8–30 ms) → facilitation.
Clinical Role: Research into cortical inhibition/facilitation, not routine therapy.

3. Repetitive TMS (rTMS)

Definition: Trains of pulses designed to produce neuroplastic changes that outlast stimulation.
Types:
Low-Frequency (LF-rTMS): ≤1 Hz; reduces cortical excitability (*LTD-like effect*).
High-Frequency (HF-rTMS): >5–20 Hz; increases cortical excitability (*LTP-like effect*).

Typical Clinical Targets:

Frequency	Effect	Common Targets	Example Indications
1 Hz	Inhibitory	Right DLPFC	Anxiety, auditory hallucinations
10 Hz	Excitatory	Left DLPFC	Depression
20 Hz	Excitatory	SMA, motor cortex	Negative symptoms in schizophrenia

4. Patterned Protocols

4.1 Theta Burst Stimulation (TBS)

- Principle: Mimics natural theta rhythm (5 Hz) associated with learning and memory.
- Pulse structure: Bursts of 3 pulses at 50 Hz, repeated at 5 Hz.
- Forms:
    - Intermittent TBS (iTBS): 2 s trains repeated every 10 s → Facilitatory.
    - Continuous TBS (cTBS): Continuous 40 s train → Inhibitory.
    - Intermediate TBS (imTBS): Mixed protocol; under research.
- Advantages: Shorter sessions (~3–10 min), non-inferior to conventional HF in depression.

4.2 Quadri-Pulse Stimulation (QPS)

- Pulse structure: Four pulses with fixed inter-pulse interval (e.g., 5 ms → facilitation; 50 ms → inhibition).
- Status: Primarily research; potential future clinical applications.

5. Accelerated Protocols

- Definition: Multiple sessions per day over a shorter total treatment duration.
- Example: SAINT protocol – iTBS to left DLPFC, 10 sessions/day for 5 days; >80% remission in TRD in open-label trial.
- IPS 2023 Note: Evidence promising but limited; should be restricted to research settings until replicated in large RCTs.

6. Bilateral & Sequential Protocols

- Bilateral: Combines HF to one hemisphere and LF to the contralateral side (e.g., HF-LDLPFC + LF-RDLPFC in depression).
- Sequential priming rTMS: LF “priming” before HF to enhance plasticity.

7. Site-Specific Paradigm Examples

Target Site	Frequency	Protocol	Common Indications
Left DLPFC	10 Hz / iTBS	HF-rTMS / iTBS	Depression, TRD
Right DLPFC	1 Hz / cTBS	LF-rTMS / inhibitory TBS	Anxiety, PTSD
SMA	1 Hz	LF-rTMS	OCD, Tourette's
Right TPJ	1 Hz	LF-rTMS	Auditory hallucinations
Cerebellum	HF	HF-rTMS	Ataxia, tremor (experimental)

8. IPS 2023 Safety Parameters

- Within safety limits defined by Rossi et al. (2009) for conventional rTMS; patterned protocols have separate, stricter limits.
- First 3 sessions carry highest seizure risk — monitor closely.
- Ear protection mandatory for all present.
- Avoid acute intoxication, withdrawal states, uncontrolled medical conditions before stimulation.

" Choice of paradigm depends on diagnosis, target symptoms, available equipment, and patient tolerability. For standardisation, document frequency, pulses per session, train duration, inter-train interval, total sessions, and coil type in the medical record."

Chapter 5

Clinical Target Localisation

Accurate localisation of the stimulation target is critical for optimising rTMS efficacy and reproducibility.
Targeting methods range from simple scalp-based measurements to advanced image-guided neuronavigation.

1. Scalp-Based Methods

a. 5-cm Rule

- Identify the motor hotspot for the contralateral abductor pollicis brevis (APB) muscle.
- Measure 5 cm anterior along a parasagittal line to approximate the left dorsolateral prefrontal cortex (LDLPFC).
- Limitations: Does not account for individual brain size or cortical folding; risk of targeting premotor cortex.

b. International 10–20 EEG System

- Uses cranial landmarks: nasion, inion, and pre-auricular points.
- Positions are proportionally spaced according to skull size.
- Key target points:
    - F3: Approximate LDLPFC
    - F4: Approximate RDLPFC
    - CZ: Vertex
    - C3/C4: Primary motor cortex
- Advantages: Cost-effective, reproducible, widely used in clinical settings.

2. MRI-Guided Neuronavigation

- Uses structural MRI to map scalp location to underlying cortical anatomy.
- Real-time optical tracking ensures the coil is positioned and oriented precisely at the target throughout the session.
- Benefits: Improves reproducibility, especially in research and treatment-resistant depression.
- Limitations: Higher cost, requires dedicated hardware/software.

3. Functional and Connectivity-Based Targeting *(2025 Emerging Standard)*

- Functional MRI (fMRI): Targets regions showing altered activity (task-based or resting state).
- Resting-State Functional Connectivity (RSFC): Identifies subregions of DLPFC most anticorrelated with subgenual anterior cingulate cortex (sgACC) for depression.
- Diffusion Tensor Imaging (DTI): Guides targeting of white matter tracts connected to symptom-relevant networks.
- Connectome-Guided TMS: AI algorithms match patient-specific brain network topology to optimal stimulation sites.

4. Other Imaging-Based Approaches

- PET/SPECT: Identify hypometabolic or hypoperfused cortical areas.
- fNIRS-Assisted Localisation: Uses cortical haemodynamic responses to confirm activation during stimulation — gaining traction in portable setups.

5. Special Targets in Psychiatry

Disorder / Symptom	Common Target	Notes
Major Depressive Disorder	LDLPFC (F3)	HF or iTBS
Anxiety Disorders / PTSD	RDLPFC (F4)	LF or cTBS
OCD	SMA (FCz) / RDLPFC / LDLPFC	Bilateral or unilateral
Schizophrenia (Auditory Hallucinations)	Left TPJ (T3–P3)	LF 1 Hz
Craving / Substance Use	LDLPFC	HF or deep TMS
Tinnitus	Auditory cortex / TPJ	LF 1 Hz

6. Coil Orientation and Positioning

- Standard for DLPFC: Coil handle angled ~45° posterior–lateral to midline, inducing posterior–anterior current.
- SMA: Coil centred over FCz, handle pointing posteriorly.
- Maintain consistent coil placement across sessions using scalp marks, caps, or neuronavigation.

7. Documentation

For every session, record:

- Target site and localisation method.
- Coil type and orientation.
- Motor threshold (% of stimulator output).
- Session parameters (frequency, trains, pulses, inter-train interval).

While 10–20 EEG mapping remains acceptable in routine clinical use, neuronavigation and connectivity-guided targeting are rapidly becoming the precision standard for complex or treatment-resistant cases.

Chapter 6

Consensus Recommendations & Safety Guidelines

Safe and effective delivery of rTMS requires adherence to international consensus standards and national guidelines. These recommendations cover the treatment environment, operator qualifications, patient preparation, and risk mitigation.

1. Clinical Environment

- Adequate space for rTMS device, coil positioning, and patient seating.
- Operator must have direct line-of-sight to the patient throughout the session.
- Maintain room temperature to prevent device overheating.
- All present (patient and staff) must wear hearing protection providing ≥30 dB noise reduction.
- Avoid distractions — patients should remain still, avoid speaking on the phone, and not eat or drink during sessions.

2. Personnel & Training

- TMS Physician:
    - Licensed clinician (psychiatry, neurology, or neurosurgery) with formal training in rTMS.
    - Knowledgeable in brain physiology, rTMS protocols, side-effect recognition, and seizure management.
- TMS Operator:
    - Can be trained non-medical or paramedical staff (nurse preferred).
    - Must be able to recognise adverse effects, assist in emergency management, and maintain coil placement accuracy.
- Training:
    - IPS, NIMHANS, AIIMS, and other centres conduct certified rTMS training programs for both clinicians and technicians.

3. Documentation in Medical Records

Include:

- Diagnosis and indication for rTMS.
- Device and coil type.
- Localisation method and cortical site.
- Motor threshold (% of stimulator output).
- Stimulation parameters (frequency, train duration, inter-train interval, pulses/session).
- Side effects and adverse events.
- Concurrent medications and dose changes during treatment.

4. Contraindications & Cautions

Absolute Contraindications:

- Ferromagnetic or magnet-sensitive implants in head/neck (except titanium).
- Cochlear implants, deep brain stimulation leads <10 cm from coil.
- Pacemakers or neurostimulators <10 cm from stimulation site.

Relative Contraindications / Require Risk–Benefit Assessment:

- History of epilepsy or seizures (patient or family).
- Structural brain lesions (tumours, malformations).
- Recent significant head trauma or intracranial surgery.
- Medications lowering seizure threshold (e.g., clozapine, bupropion) — proceed with caution.

5. Pre-Treatment Screening: TMS Adult Safety Screen (TASS)

Instructions: Ask each question. Mark “Yes” or “No”. For any “Yes” answer, record details and consult with TMS physician to determine risk–benefit ratio.
(Adapted from Rossi et al., 2009; Keel et al., 2001)

No.	Question	Yes / No	Details if “Yes”
1	Do you have epilepsy, or have you ever had a seizure?		
2	Have you ever had a fainting spell or syncope?		
3	Have you ever had a head injury that caused loss of consciousness?		
4	Do you have any hearing problems or ringing in your ears (tinnitus)?		
5	Are you pregnant or could you be pregnant?		
6	Do you have any metal in your head, skull, or neck (excluding titanium), such as surgical clips, fragments, splinters, plates, or wires?		
7	Do you have a cochlear implant or other implanted hearing device?		
8	Do you have an implanted neurostimulator (deep brain, spinal cord, vagal nerve)?		

9	Do you have a cardiac pacemaker, intracardiac lines, or other implanted cardiac devices?		
10	Do you have a medication infusion pump (e.g., for insulin, baclofen)?		
11	Are you taking any medications? (List all, including doses)		
12	Have you had surgery involving your spinal cord?		
13	Do you have any ventricular or lumbar drains?		
14	Have you ever had TMS before? If yes, any side effects?		
15	Have you ever had MRI before? If yes, any problems?		
16	Do you have any tattoos containing metallic or ferromagnetic ink near the stimulation site?		
17	Have you used alcohol, recreational drugs, or nicotine within the last 24 hours?		

CPG-IPS 2023 Note:

- Affirmative answers do not always mean exclusion — they require individualised assessment.
- Additional paediatric questions and operator safety questions are recommended when treating younger patients or running high-volume clinics.

6. Patient Preparation

- Adequate sleep prior to session.
- Avoid acute alcohol, nicotine, caffeine, or illicit substance use before treatment.
- Ensure no acute medical instability (fever, uncontrolled hypertension, acute infection, fresh scalp injury).
- Remove metallic hair accessories or jewellery near coil placement site.

7. Determining Motor Threshold (MT)

- Define MT before first session, reassess weekly or if clinical/medication status changes.
- IPS Definition: Minimum stimulator output that elicits visible muscle twitch in ≥5 of 10 trials in APB muscle, or EMG-detected MEP.

8. Safety Precautions During Stimulation

- First 3 sessions have highest seizure risk — monitor closely.
- Maintain coil–implant distance ≥10 cm if patient has non-cranial devices.
- Start at subthreshold intensity in special populations, titrate up as tolerated.
- Use earplugs for both operator and patient for every session.

9. Special Populations

- Paediatrics: Safe in children ≥2 years for single/paired-pulse; limited therapeutic rTMS data — use with caution.
- Pregnancy: Minimal fetal exposure with standard coils; considered safe for mother and child in depression protocols.
- Elderly: Monitor for discomfort, hearing issues, or orthostatic symptoms.

10. Emergency Preparedness

- Keep anticonvulsants (e.g., diazepam, lorazepam) readily available.
- Have a seizure management protocol posted in the room.
- Ensure trained staff present for every session.

Chapter 7

Clinical Evidence & Applications

1. Major Depressive Disorder (MDD) & Treatment-Resistant Depression (TRD)

Evidence Strength: ★★★★☆ (Strong)
Best Supported Protocols:

Protocol	Target	Frequency	Pulses/Session	Duration	Notes
HF-rTMS	Left DLPFC	10 Hz	3,000–4,000	20–30 min	Most robust evidence; FDA-approved
LF-rTMS	Right DLPFC	1 Hz	1,200–1,800	20 min	Alternative in anxiety-prone patients
Bilateral	L-DLPFC + R-DLPFC	HF + LF	Combined	30–40 min	For severe TRD
iTBS	Left DLPFC	50 Hz bursts @ 5 Hz	600	~3 min	Non-inferior to HF-rTMS; FDA-approved

Special Notes:

- Maintenance protocols (weekly → monthly) may reduce relapse risk.
- Accelerated TBS (e.g., SAINT) promising but requires further validation.

2. Bipolar Depression

Evidence Strength: ★★☆☆☆ (Moderate)

- HF-rTMS over left DLPFC shows benefit; LF and bilateral protocols less consistent.
- Avoid use during mania unless specifically targeting right DLPFC for inhibitory effect.

3. Peripartum & Postpartum Depression

Evidence Strength: ★★☆☆☆ (Moderate)

- Safe for mother and infant.
- HF-LDLPFC more effective than LF-RDLPFC.

4. Post-Stroke Depression

Evidence Strength: ★★★☆☆ (Strong for mood, limited for cognition)

- HF-LDLPFC most supported; significant improvement in depressive symptoms.

5. Generalized Anxiety Disorder (GAD)

Evidence Strength: ★★★☆☆ (Moderate–Strong)

Protocol	Target	Frequency	Notes
LF-rTMS	Right DLPFC	1 Hz	Most evidence for anxiety reduction
HF-rTMS	Right DLPFC	10–20 Hz	Alternative; fewer studies

6. Post-Traumatic Stress Disorder (PTSD)

Evidence Strength: ★★★☆☆ (Moderate)

- HF or LF over right DLPFC both effective; no clear superiority.
- Bilateral stimulation may be considered in refractory cases.

7. Obsessive-Compulsive Disorder (OCD)

Evidence Strength: ★★★☆☆ (Moderate)

Protocol	Target	Frequency	Pulses	Duration	Notes
LF-rTMS	Right DLPFC	1 Hz	1,200–1,800	20 min	Good global improvement
HF-rTMS	Bilateral DLPFC	10 Hz	2,000–3,000	20–30 min	Robust but variable
LF-rTMS	SMA	1 Hz	1,200–1,800	20 min	Effective for compulsions

8. Schizophrenia

Resistant Auditory Hallucinations
Evidence Strength: ★★☆☆☆ (Moderate)

- LF (1 Hz) to left temporoparietal junction (T3–P3) reduces hallucinations.

Negative Symptoms
Evidence Strength: ★★★☆☆ (Moderate–Strong)

- HF-LDLPFC (>100% MT, >7,500 stimuli/week) most effective.

9. Substance Use Disorders

Evidence Strength: ★★☆☆☆ (Moderate for nicotine & some illicit drugs; low for alcohol)

Target	Frequency	Effect
LDLPFC	HF (10–20 Hz)	Reduces craving & consumption in nicotine, cocaine
Bilateral DLPFC / Insula (deep TMS)	HF	Reduces nicotine/alcohol use in some studies

10. Chronic Pain & Migraine

Evidence Strength: ★★★☆☆ (Moderate)

- HF to motor cortex (M1) for neuropathic pain;
- HF-LDLPFC for migraine prevention (FDA-cleared for some devices).

11. Neurodevelopmental Disorders

- Autism Spectrum Disorder (ASD): Moderate improvements in social behaviour and repetitive behaviours; protocols still experimental.
- ADHD: Insufficient therapeutic rTMS data; mostly diagnostic/physiological studies.

12. Safety Profile Across Conditions

- No increased risk of serious adverse events vs sham in large meta-analyses.
- Most common: headache, scalp discomfort, facial muscle twitching — generally transient.
- Seizure risk <0.1% with guideline-adherent protocols.

Chapter 8

Commonly Used Protocols, Patient Selection & Screening, and Procedure Workflow

8.1 Introduction

Repetitive Transcranial Magnetic Stimulation (**rTMS**) has evolved from an experimental neurophysiological tool to an evidence-based therapeutic modality across psychiatric, neurological, and neurorehabilitation domains. Its clinical efficacy hinges on three interrelated pillars:

1. **Protocol optimisation** – Selection of stimulation frequency, train structure, pulse count, intensity, and target location that is best aligned with the underlying pathophysiology, symptom dimensions, and cortical circuitry of the disorder.

2. **Rigorous patient selection and screening** – Comprehensive evaluation to confirm indication, assess potential contraindications, and optimise safety.

3. **Standardised procedural workflow** – A reproducible stepwise method that minimises operator variability, improves treatment fidelity, and facilitates multi-centre research comparability.

Why integration matters:
Evidence shows that even minor deviations in coil placement, motor threshold calibration, or train timing can significantly alter cortical activation patterns and clinical outcomes (Rossi et al., 2021). Thus, **protocol choice, patient screening, and procedural standardisation** must be viewed as a single, interdependent process.

This chapter presents a **framework for rTMS delivery** that incorporates **Indian Psychiatric Society (IPS) 2023 Clinical Practice Guidelines**, **international consensus statements** (Lefaucheur et al., 2020; Perera et al., 2016), and recent meta-analytic evidence. For each major rTMS paradigm, we summarise efficacy data, dosing ranges, and levels of evidence.

8.2 Commonly Used Protocols

rTMS protocols are defined by **frequency of stimulation**, **pattern of pulse delivery**, **anatomical target**, and **total treatment course**. Each combination has specific neurophysiological effects:

- **High-frequency (>5 Hz)**: Generally increases cortical excitability through **LTP-like plasticity**.

- **Low-frequency (≤1 Hz)**: Generally reduces cortical excitability via **LTD-like plasticity**.

- **Patterned stimulation (e.g., TBS)**: Attempts to replicate endogenous brain rhythms to efficiently modulate synaptic strength.

8.2.1 High-Frequency (HF) Stimulation

- **Frequency:** 5–20 Hz (commonly 10 Hz)
- **Target:** Left dorsolateral prefrontal cortex (**LDLPFC**, F3 in the 10–20 EEG system)
- **Mechanism:** Enhances prefrontal network excitability, increases synaptic efficacy via **NMDA receptor–dependent LTP-like mechanisms**, modulates limbic-prefrontal connectivity.
- **Clinical Indications:**
    - **Primary:** Major depressive disorder (MDD), especially treatment-resistant depression (TRD)
    - **Secondary:** Negative symptoms of schizophrenia, mild cognitive impairment, early Alzheimer's disease (adjunctive)
- **Typical Parameters:**
    - 3,000–4,000 pulses/session
    - 20–30 trains
    - Intertrain interval (ITI): 20–30 seconds
    - Intensity: 100–120% of resting motor threshold (RMT)

Evidence Summary: HF rTMS (LDLPFC)	
Key RCTs / Meta-Analyses	George et al., 2010 (NEJM); Berlim et al., 2014; Lefaucheur et al., 2020
Effect Size	Depression: Hedges' g ≈ 0.39–0.55; Schizophrenia (negative symptoms): g ≈ 0.28
Response / Remission Rates	29–46% (response), 18–30% (remission) in TRD
Recommended Dosing Range	3,000–4,000 pulses/day × 20–30 sessions
Level of Evidence (GRADE)	**High** for depression; **Moderate** for schizophrenia

8.2.2 Low-Frequency (LF) Stimulation

- **Frequency:** 1 Hz
- **Target:** Right DLPFC (F4) in depression; contralesional primary motor cortex (M1) in stroke rehabilitation
- **Mechanism:** Reduces cortical hyperactivity via **GABA-mediated LTD-like mechanisms**, rebalances interhemispheric asymmetry.
- **Clinical Indications:**
    - Depression with marked anxiety features
    - Post-stroke motor recovery (contralesional inhibition)
    - Chronic pain modulation
- **Typical Parameters:**
    - 1,200–1,800 pulses/session
    - Continuous trains (no ITI)
    - 90–100% RMT

Evidence Summary: LF rTMS (Right DLPFC / Contralesional M1)	
Key RCTs / Meta-Analyses	Fitzgerald et al., 2003; Lefaucheur et al., 2020; Hsu et al., 2012
Effect Size	Depression: g ≈ 0.30–0.40; Stroke motor recovery: g ≈ 0.35–0.50
Response / Remission Rates	25–35% response in depression
Recommended Dosing Range	1,200–1,800 pulses/day × 20–30 sessions
Level of Evidence (GRADE)	**Moderate** for depression; **High** for stroke rehabilitation

8.2.3 Theta Burst Stimulation (TBS)

- **Principle:** Mimics endogenous hippocampal-prefrontal theta rhythms (~5 Hz) that promote synaptic plasticity.
- **Structure:** Bursts of 3 pulses at 50 Hz every 200 ms.
- **Variants:**
    - **Intermittent TBS (iTBS)** – Excitatory; 2 s train / 8 s pause; ~600 pulses; session duration ~3 min
    - **Continuous TBS (cTBS)** – Inhibitory; continuous 40 s train; ~600 pulses
- **Advantages:** Session duration reduced from ~37 min (HF) to ~3 min (iTBS) with comparable clinical outcomes (Blumberger et al., 2018).

Evidence Summary: TBS	
Key RCTs / Meta-Analyses	Blumberger et al., 2018 (THREE-D Trial); Chung et al., 2016
Effect Size	Depression (iTBS vs HF): non-inferior; g ≈ 0.37–0.45
Session Duration	3 min (iTBS) vs ~37 min (HF)
Recommended Dosing Range	iTBS: 600 pulses/session × 20–30 sessions
Level of Evidence (GRADE)	**High** for depression

8.2.4 Bilateral Stimulation

- **Approach:** Sequential or alternating HF to LDLPFC and LF to RDLPFC.
- **Rationale:** Addresses hemispheric imbalance in mood disorders by increasing left and reducing right prefrontal activity.
- **Indications:** TRD, cognitive disorders with hemispheric asymmetry.

Evidence Summary: Bilateral rTMS	
Key RCTs / Meta-Analyses	Fitzgerald et al., 2006; Lefaucheur et al., 2020
Effect Size	Depression: g ≈ 0.45–0.50
Response / Remission Rates	35–50% response
Recommended Dosing Range	HF 3,000 pulses (LDLPFC) + LF 1,200 pulses (RDLPFC)
Level of Evidence (GRADE)	**Moderate**

8.2.5 Target-Specific Protocols

Target Site	Frequency	Typical Indications	Evidence Summary
M1	HF or LF	Neuropathic pain, motor recovery post-stroke	Lefaucheur et al., 2020; Pain relief: g ≈ 0.30–0.45
SMA (FCz)	1 Hz	OCD, Tourette's, Parkinson's	Mantovani et al., 2010; OCD severity reduction: g ≈ 0.35
TPJ	1 Hz	Auditory hallucinations in schizophrenia	Slotema et al., 2014; Hallucination reduction: g ≈ 0.44
OFC (Fp1/Fp2)	HF or LF	OCD, addiction	Hawken et al., 2016; Preliminary evidence: g ≈ 0.25–0.30

8.3 Patient Selection & Screening

Patient selection is critical to both safety and efficacy. Inappropriate selection increases the risk of adverse events and may dilute treatment effects in clinical trials. Screening should be systematic, documented, and protocol-driven.

8.3.1 Indication Confirmation

- Use **ICD-11** or **DSM-5** criteria for diagnosis.
- For **major depressive disorder**, confirm *treatment resistance*: inadequate response to ≥2 adequate antidepressant trials (minimum 6–8 weeks at therapeutic dose) or intolerance to standard pharmacotherapy.
- For other conditions (OCD, chronic pain, post-stroke rehabilitation), ensure diagnosis is based on validated criteria (e.g., Y-BOCS ≥ 24 for OCD).

Decision Point:
If diagnosis is unclear or psychiatric comorbidity may affect adherence, consider a stabilisation phase before rTMS initiation.

8.3.2 Baseline Clinical Assessment

Domain	Tool/Scale	Purpose
Symptom severity	HDRS, MADRS, Y-BOCS, PANSS, GAD-7	Outcome measurement and response tracking
Cognition	MoCA, MMSE	Baseline cognitive function (important for dementia trials)
Function	WHODAS 2.0, GAF	Assess disability and recovery trajectory
Quality of life	WHOQOL-BREF	Captures broader treatment benefits

8.3.3 Contraindications

- **Absolute:**
    - Active seizure disorder or uncontrolled epilepsy
    - Ferromagnetic intracranial implants or aneurysm clips
    - Implanted medical devices <10 cm from coil path that are not MRI-conditional
- **Relative:**
    - Pregnancy (safety data limited but emerging)
    - Unstable cardiovascular status
    - Severe behavioural dysregulation or personality disorder likely to impair adherence

8.3.4 Safety Screening

- Administer **TMS Adult Safety Screen (TASS)** before first session.
- Document:
    - Seizure risk factors (personal/family history, TBI, brain lesions)
    - Hearing status (recommend baseline audiometry for high-intensity or paediatric protocols)
    - Implanted devices or metallic foreign bodies

8.3.5 Informed Consent

Must include:

- **Expected latency of response:** 2–4 weeks in depression, variable in other disorders
- **Common side effects:** Scalp discomfort, headache, transient facial muscle twitching
- **Rare events:** Seizure risk (<0.1% with adherence to guidelines), syncope, mood switching in bipolar depression
- **Treatment commitment:** Daily sessions for 4–6 weeks for most protocols

8.4 Procedure Workflow

A consistent procedural workflow is essential for reproducibility, especially in multi-centre trials and high-volume clinical settings.

8.4.1 Pre-Session Preparation

1. **Patient verification** – Name, date of birth, diagnosis, consent.
2. **Remove metallic/conductive items** – Jewellery, hairpins, credit cards, hearing aids if applicable.
3. **Positioning** – Reclined or upright chair, head supported, neck relaxed.
4. **Ear protection** – Mandatory for patient; strongly advised for operator.

8.4.2 Motor Threshold (MT) Determination

- Identify the **motor hotspot** for the contralateral abductor pollicis brevis (APB).
- Define **Resting Motor Threshold (RMT)**: Lowest stimulator output producing MEP ≥50 μV in ≥50% of 10 trials.
- Reassess MT:
    - Weekly
    - After medication changes affecting cortical excitability
    - If clinical status changes significantly

8.4.3 Target Localisation

- **Standard method:** 10–20 EEG system (e.g., F3 for LDLPFC)
- **Optimal method:** MRI-guided neuronavigation for anatomical precision
- **Coil orientation:** ~45° posterior–lateral to the midline for DLPFC; adjust for other targets
- **Contact pressure:** Consistent across sessions to avoid variability in depth of stimulation.

8.4.4 Stimulation Delivery

- Follow **protocol-specific parameters** (frequency, pulses, train duration, ITI, intensity).
- Monitor for signs of discomfort, excessive muscle twitching, or prodromal seizure symptoms.

- Avoid session interruptions unless medically necessary.

8.4.5 Post-Session Monitoring

- Observe for ≥5 minutes for adverse events.
- Document:
    - Target site and localisation method
    - MT and stimulation parameters
    - Patient's subjective response and any adverse effects
- Reinforce adherence and confirm next appointment.

8.5 Clinical Practice Pearls

- **Evidence-based targeting** improves efficacy — avoid "one-size-fits-all" approaches.
- **Objective MT determination** ensures dosing accuracy and minimises under/overstimulation.
- **Protocol fidelity** is essential for reproducibility — use treatment logs.
- **Patient engagement** improves adherence — educate about expected time to benefit.
- **Side-effect mitigation:** Adjust coil position or intensity for scalp discomfort; stagger train onset for sensitive patients.

Chapter 9

Patient Selection & Screening

9.1 Introduction

Patient selection is a primary determinant of repetitive Transcranial Magnetic Stimulation (**rTMS**) safety, tolerability, and therapeutic success. Although rTMS is well-tolerated and non-invasive, benefits are maximised when delivered to appropriately screened individuals. This chapter provides a structured approach to determining suitability, identifying contraindications, assessing readiness, and documenting baseline parameters before therapy—now integrated with **comparative positioning versus alternative treatments** for the same indications.

9.2 Goals of Screening

- **Ensure safety:** Exclude or mitigate risks (seizure, implanted devices, unstable medical illness).
- **Maximise efficacy:** Select patients most likely to benefit based on diagnosis, history, and symptom profile.
- **Set expectations:** Realistic timelines, side effects, and outcomes.
- **Standardise procedures:** Align with IPS 2023 guidance and international consensus.

9.3 Indication Confirmation

Diagnostic framework: ICD-11 or DSM-5.

Regulatory psychiatric indications:

- Major Depressive Disorder (MDD; including TRD)
- Obsessive–Compulsive Disorder (OCD)
- Smoking cessation
- Migraine prevention

Evidence-supported off-label:

- Generalised Anxiety Disorder (GAD), Post-Traumatic Stress Disorder (PTSD)
- Post-stroke depression and motor rehabilitation

- Schizophrenia (negative symptoms, auditory hallucinations)
- Chronic pain syndromes
- Selected neurodevelopmental/neurodegenerative disorders

9.4 Establishing Treatment Resistance

Disorder	Treatment-resistance threshold (typical)
MDD	≥2 adequate antidepressant trials (different classes; dose/duration adequate)
OCD	≥2 adequate SSRI/clomipramine trials ± ERP
Schizophrenia (negative symptoms)	Optimised antipsychotic care ≥6 months

Documentation: Antidepressant Treatment History Form (ATHF) where applicable.

9.5 Baseline Clinical Assessment

Domain	Tool	Purpose
Symptom severity	HDRS/MADRS, Y-BOCS, PANSS, GAD-7	Baseline & outcomes
Cognition	MoCA, MMSE	Particularly in elderly/cognitive targets
Function	WHODAS 2.0, GAF	Disability/trajectory
Medical comorbidity	History, exam, labs as indicated	Risk assessment
Psychiatric comorbidity	Structured interview	Adherence risk, safety

9.6 Contraindications

Absolute:

- Active seizure disorder/uncontrolled epilepsy (unless risk–benefit strongly favourable under expert supervision)
- Ferromagnetic/magnet-sensitive cranial implants (excluding dental fillings)
- Non-MRI-compatible implanted devices <10 cm from coil path

Relative:

- Pregnancy (increasing safety data; proceed with caution)
- Unstable cardio-respiratory/metabolic status
- Severe behavioural dysregulation impacting adherence
- Recent significant head injury/neurosurgery
- Drugs lowering seizure threshold (e.g., clozapine, bupropion, high-dose TCAs): dose review and monitoring required

9.7 Safety Screening – TMS Adult Safety Screen (TASS)

Screen for seizure history/syncope, significant head injury, hearing issues/tinnitus, pregnancy, metallic fragments/implants, cochlear/other stimulators, pacemakers/infusion pumps, current medications/substance use.
Note: A "yes" is not automatic exclusion; apply an individualised risk–benefit appraisal.

9.8 Informed Consent

Content: Procedure and rationale; expected onset (often 2–4 weeks in MDD); common side effects (headache, scalp pain, facial twitching); less common (dizziness, transient mood changes); rare (<0.1% seizure with guideline adherence); typical course (20–30 weekday sessions; maintenance may follow); adjunctive nature with meds/psychotherapy.

Documentation: Signed form (patient & clinician), date, witness if required; copy to patient.

9.9 Readiness & Adherence Assessment

- **Logistics:** Daily attendance for 4–6 weeks, transport, work/family commitments
- **Motivation:** Understanding and commitment to complete course
- **Support:** Family/caregiver facilitation and monitoring

Pre-treatment counselling improves completion and outcomes.

9.10 Pre-Treatment Preparations

Adequate sleep; avoid acute alcohol, high caffeine/nicotine, or illicit drugs pre-session; remove metallic hair accessories/jewellery; ensure vitals are acceptable.

9.11 Documentation Checklist

- Diagnosis/indication; baseline scales; cognitive screen (if relevant)
- Contraindication screening outcome (TASS)
- Informed consent completed
- Planned protocol and parameters; RMT measurement plan

9.12 Comparative Effectiveness & Clinical Positioning (rTMS vs Alternatives)

How to use this section: For each indication, compare rTMS with other validated options on **onset**, **response/remission**, **durability/maintenance**, **adverse-effect burden**, **resource intensity**, and **setting**. End with **"When to prefer rTMS"** to support shared decision-making.

9.12.1 Major Depressive Disorder (incl. TRD)

Modality	Onset	Response / Remission (typical ranges)	Durability & Maintenance	Adverse Effects	Setting/Intensity
rTMS (HF LDLPFC / iTBS)	2–4 weeks; iTBS similar	~30–50% / ~20–30% in TRD	Good with continuation/maintenance; relapse ↓ with scheduled boosters	Scalp pain, headache; seizure rare	Outpatient; daily for 4–6 weeks
ECT	Days–2 weeks	60–80% / 40–60% (highest for severe/psychotic MDD)	Strong durability with continuation ECT/meds	Post-ictal confusion, cognitive side effects, anaesthesia	Inpatient/outpatient anaesthesia; high resource
IV ketamine / IN esketamine	Hours–days	~40–70% short-term response	Benefit often wanes without maintenance dosing	Dissociation, ↑BP/HR, nausea; misuse potential	Monitored setting; frequent visits

Pharmacotherapy (third-line/augmentation)	Weeks	Variable; diminishing returns after ≥2 failures	Maintenance feasible; adherence limits	Systemic AEs (GI, sexual, weight, metabolic, QT)	Outpatient; ongoing
CBT / IPT	Weeks–months	Mild–moderate MDD responsive; lower in TRD	Durable skills; relapse prevention	Minimal	Outpatient; weekly

When to prefer rTMS: TRD without need for rapid rescue; patient declines/at risk with ECT or ketamine; polypharmacy intolerance; outpatient, cognition-sparing priority; suitable for maintenance/booster strategies.

9.12.2 Obsessive–Compulsive Disorder (OCD)

Modality	Onset	Response	Durability	Adverse Effects	Notes
rTMS (SMA, OFC, or DLPFC targets; 1 Hz or HF/iTBS)	3–6 weeks	Modest–moderate Y-BOCS reduction	Improved with consolidation/maintenance	Scalp discomfort, headache	Target selection matters (SMA/OFC evidence growing)
ERP-based CBT	Weeks–months	Strong efficacy; first-line	Durable with practice	Exposure distress	Access/training dependent
SSRIs / Clomipramine	Weeks	Moderate	Maintenance feasible	Sexual/anticholinergic, QTc (clomipramine)	Often combined with ERP
DBS (refractory)	Months	Substantial in ultra-refractory	Durable with programming	Surgical risks, hardware	Reserved for severe refractory cases

When to prefer rTMS: Partial/non-responders to SSRI/ERP; augmentation to ERP; patients preferring non-systemic options; pre-DBS step.

9.12.3 Smoking Cessation

Modality	Efficacy	Durability	Adverse Effects	Notes
rTMS (DLPFC; HF/iTBS)	Reduced craving; quit-rate benefit in structured protocols	Booster sessions helpful	Minimal	Useful adjunct to pharmacotherapy
Varenicline	Highest single-agent quit rates	Good with full course	Nausea, vivid dreams	First-line
NRT (patch/gum/lozenge)	Moderate; better in combinations	Requires adherence	Local irritation	Accessible
Bupropion	Moderate	Good with full course	Insomnia, seizure risk (rare)	Also treats low mood

When to prefer rTMS: Medication intolerance/contraindication; refractory craving; as an adjunct to varenicline/NRT in high-dependence smokers.

9.12.4 Migraine Prevention

Modality	Efficacy	Onset	Adverse Effects	Notes
rTMS (M1/DLPFC protocols)	Reduction in frequency/intensity (modest-moderate)	Weeks	Minimal	Non-systemic option
CGRP mAbs	High efficacy	Weeks	Injection reactions, constipation	Costly but convenient monthly
Topiramate / Valproate	Moderate-high	Weeks	Cognitive slowing, weight change, teratogenicity (valproate)	Systemic AEs
OnabotulinumtoxinA (chronic)	Reduces headache days	Weeks	Injection site pain	For chronic migraine

When to prefer rTMS: Patients avoiding systemic AEs, women planning pregnancy, multi-drug intolerance, adjunct where mAbs unaffordable/unavailable.

9.12.5 PTSD & GAD

Modality	Efficacy	Onset	Durability	Adverse Effects
rTMS (DLPFC; HF/iTBS or right-sided LF)	Symptom reduction (moderate in PTSD; modest–moderate in GAD)	Weeks	Maintenance/booster helpful	Minimal
Trauma-focused CBT/EMDR (PTSD)	High	Weeks–months	Durable skills	Exposure distress
SSRIs/SNRIs	Moderate	Weeks	Maintenance possible	Systemic

When to prefer rTMS: Poor medication tolerance; partial responders to psychotherapy seeking augmentation; preference for non-systemic therapy.

9.12.6 Schizophrenia

Negative symptoms

Modality	Efficacy	Notes
rTMS (HF left DLPFC)	Small–moderate improvement	Safe adjunct; effect sizes modest
Optimised antipsychotics / psychosocial rehab	Foundation of care	Clozapine for refractory
tDCS (fronto-temporal)	Emerging modest effect	Low-intensity option

Auditory hallucinations

Modality	Efficacy	Notes
rTMS (1 Hz TPJ; left or bilateral)	Moderate reduction in hallucination severity	Best in persistent, treatment-resistant AH
Clozapine / CBT for psychosis	Standard	May combine with rTMS

When to prefer rTMS: Persistent negative symptoms/AH despite adequate antipsychotic trials (including clozapine) and psychosocial interventions; patient preference for non-pharmacologic adjuncts.

9.12.7 Post-Stroke Motor Rehabilitation / Post-Stroke Depression

Modality	Target	Efficacy	Notes
rTMS (LF contralesional M1 / HF ipsilesional M1)	Interhemispheric rebalance	Moderate gains in motor function	Best when embedded in task-oriented rehab
Conventional rehab	Intensive therapy	Foundation of gains	Combine with rTMS
SSRIs (post-stroke depression)	Mood benefit	Standard where indicated	Monitor hyponatraemia/bleeding risk in elderly

When to prefer rTMS: As an adjunct to structured physio-rehab; patients unable to escalate meds due to AEs; post-stroke depression with polypharmacy concerns.

9.12.8 Chronic Pain Syndromes

Modality	Target	Efficacy	Notes
rTMS (M1; HF/iTBS)	Sensorimotor modulation	Small–moderate analgesic effect	Series + boosters often needed
Pharmacologic (duloxetine, pregabalin, TCAs, opioids)	Systemic	Variable; AE trade-offs	Opioid stewardship critical
CBT-pain, physio	Behavioural/functional	Durable skill benefits	Combine

When to prefer rTMS: Medication intolerance, desire to minimise opioids, neuropathic features, adjunct to multimodal pain rehab.

9.12.9 Neurodegenerative & Neurodevelopmental

- **Mild Cognitive Impairment / early Alzheimer's:** rTMS (DLPFC/parietal networks) shows modest cognitive benefits; combine with cognitive training.

- **Tourette's / Parkinson's:** rTMS over SMA/motor regions yields symptom reduction in selected patients; combine with standard care.

When to prefer rTMS: Patients prioritising cognition-sparing, non-systemic options; as adjuncts where meds are limited by AEs.

9.12.10 Practical Sequencing & Shared Decision-Making

1. **Start with guideline-endorsed first-line(s)** for the indication.

2. **Offer rTMS** when:

    - ≥2 adequate medication/therapy failures or intolerance

    - Desire to avoid anaesthesia/cognitive AEs (vs ECT) or systemic AEs (vs meds)

    - Outpatient, cognition-sparing, maintenance-friendly strategy is preferred

3. **Use head-to-head considerations:**

    - **Need rapid rescue?** Consider ECT/ketamine first.

    - **Cognitive preservation / driving/work continuity?** rTMS advantageous.

    - **Severe psychosis/catatonia/urgent suicidality?** ECT preferred.

4. **Plan durability:** Combine rTMS with relapse-prevention medication/psychotherapy; schedule **booster** sessions as needed.

9.12.11 Safety & Resource Considerations (Cross-Modality)

Factor	rTMS	ECT	Ketamine/Esketamine	Pharmacotherapy	Psychotherapy
Anaesthesia	No	Yes	No (monitoring required)	No	No
Cognitive AEs	Minimal	Common, transient	Minimal (dissociation)	Variable	None
Seizure risk	Rare (<0.1%)	Induced	Low	Variable	None
Setting	Outpatient	Procedure suite	Monitored clinic	Outpatient	Outpatient
Maintenance	Boosters feasible	Continuation ECT	Ongoing dosing	Ongoing	Skills practice

Key Take-Home

- A **standardised selection & screening pathway** improves safety and outcomes.
- rTMS sits **alongside** ECT, ketamine/esketamine, pharmacotherapy, and psychotherapy—not above or below them—each has a clear niche.
- Choose rTMS when you need an **outpatient, cognition-sparing, non-systemic** intervention with good durability (especially for TRD), and integrate it with maintenance strategies.

Chapter 10

Procedure Workflow

10.1 Introduction

A well-defined and reproducible procedure workflow is essential for delivering repetitive Transcranial Magnetic Stimulation (rTMS) safely and effectively. It ensures consistent targeting, optimised stimulation delivery, patient comfort, and adherence to safety protocols. This chapter outlines the operational sequence from pre-session preparation to post-session documentation, incorporating best practices from IPS 2023 guidelines and international consensus recommendations.

10.2 Objectives of a Standardised Workflow

- Consistency: Maintain reproducible coil positioning, parameters, and procedure timing across sessions.
- Safety: Minimise risk of adverse effects through careful monitoring and adherence to safety limits.
- Efficiency: Streamline treatment delivery without compromising quality.
- Documentation: Capture essential treatment data for clinical review and audit purposes.

10.3 Pre-Session Preparation

10.3.1 Patient Verification & Readiness

- Confirm patient identity using two identifiers (name, date of birth, hospital ID).
- Review informed consent and confirm willingness to proceed.
- Verify completion of TMS Adult Safety Screen (TASS) prior to first session.
- Assess readiness:
    - Adequate sleep and nutrition.
    - No acute intoxication, withdrawal states, or uncontrolled medical conditions.
    - No metallic accessories, hairpins, or jewellery near coil site.

10.3.2 Treatment Area Setup

- Ensure:
    - Quiet, distraction-free environment.
    - Treatment chair with adjustable headrest and arm support.
    - Adequate coil clearance around patient's head.
- Provide ear protection (≥30 dB attenuation) to patient and operator.

10.4 Motor Threshold (MT) Determination

10.4.1 Purpose

- Establish the minimum stimulator output required to elicit consistent motor responses, ensuring stimulation is individualised and within safety margins.

10.4.2 Method

- Identify motor "hotspot" for contralateral abductor pollicis brevis (APB).
- Define Resting Motor Threshold (RMT): lowest output evoking MEPs ≥50 μV in ≥5/10 trials (EMG) or visible thumb movement (visual method).
- Document:
    - Coil type and orientation (~45° posterior–lateral for DLPFC).
    - Stimulation intensity as % of stimulator output.
- Reassess:
    - Weekly.
    - After major medication changes.
    - If patient reports new scalp pain or headache.

10.5 Coil Placement & Targeting

10.5.1 Target Localisation

- Scalp-based: International 10–20 EEG system (e.g., F3 for LDLPFC, F4 for RDLPFC, FCz for SMA).
- Advanced: MRI-guided neuronavigation or connectivity-based targeting for precision and reproducibility.

10.5.2 Positioning

- Maintain coil tangential to scalp, consistent contact pressure, and fixed angle.
- Mark target site on scalp cap for manual positioning or save in neuronavigation system for automated repositioning.

10.6 Stimulation Delivery

10.6.1 Parameter Verification

Before initiating stimulation, confirm:

- Frequency (Hz).
- Pulses per train and number of trains.
- Inter-train interval (ITI).
- Total pulses/session.
- Intensity (% RMT).

10.6.2 During Stimulation

- Maintain direct visual contact with patient.
- Monitor for:
    - Excessive discomfort, facial twitching, eye blinking.
    - Sudden changes in responsiveness (possible seizure).
    - Signs of vasovagal reaction (pallor, sweating, nausea).
- Pause stimulation if patient reports severe pain, dizziness, or unusual symptoms.

10.7 Post-Session Monitoring

10.7.1 Immediate Observation (5–10 minutes)

- Ask about headache, dizziness, visual changes, or mood shifts.
- Check for signs of excessive fatigue or distress.

10.7.2 Documentation

Record:

1. Target site and localisation method.
2. Coil type and orientation.
3. MT (% stimulator output).
4. Protocol parameters (frequency, pulses, trains, ITI, intensity).
5. Any adverse effects and management steps taken.
6. Patient's subjective response to session.

10.7.3 Follow-Up

- Review cumulative adverse effects at subsequent sessions.
- Adjust coil positioning, intensity, or ITI if patient discomfort is recurrent.

10.8 Quality Control Measures

- Reproducibility: Use consistent head position markers or neuronavigation logs.
- Equipment Checks: Daily inspection of coil, cables, cooling system, and emergency stop function.
- Calibration: Periodic verification of stimulator output accuracy.
- Training: Annual operator certification renewal and hands-on competency checks.

Chapter 11:

Monitoring, Side Effects & Management

Purpose:
To ensure rTMS procedures are delivered with the highest safety standards, minimising risks while optimising therapeutic outcomes. This requires systematic monitoring before, during, and after each session, early detection of adverse events, and structured management protocols.

11.1 Safety Philosophy and Rationale

rTMS alters cortical excitability through rapid, repetitive electromagnetic pulses. While the technique is considered safe in trained hands, the possibility of transient or serious adverse events necessitates:

- Standardised safety screening to identify at-risk individuals.
- Real-time monitoring to detect physiological or behavioural changes early.
- Systematic documentation to guide ongoing care and future safety protocols.

Risk factors influencing safety include:

- High stimulation frequency and intensity.
- Proximity of stimulation site to seizure-prone cortex.
- Pre-existing neurological or psychiatric comorbidities.
- Use of medications that lower seizure threshold.

11.2 Pre-Session Monitoring

A. Safety Screening

1. Absolute Contraindications:
    - Ferromagnetic or electronic implants in the head/neck (except dental fillings).
    - Cochlear implants, deep brain stimulators, intracranial electrodes.
    - Uncontrolled epilepsy.
2. Relative Contraindications:
    - Pregnancy (safety data limited).

    - Cardiac pacemakers (unless clearance from cardiology).
    - History of severe head injury or neurosurgery.
3. Medication Review:
    - CNS stimulants, bupropion, tricyclics, and high-dose antipsychotics can lower seizure threshold.
4. Patient Consent:
    - Explain procedure, benefits, risks, and expected sensations.

B. Baseline Data Collection

- Resting Motor Threshold (RMT) measurement — essential for personalised dosing.
- Vital signs: BP, HR, SpO_2.
- Baseline symptom scoring (e.g., HDRS, MoCA, PANSS, depending on indication).
- Neurological examination if warranted.

11.3 Intra-Session Monitoring

A. Operator Vigilance

- Maintain direct visual contact with the patient.
- Watch for:
    - Grimacing, frowning, wincing (discomfort).
    - Excessive blinking or facial twitching (coil position or intensity issue).
    - Loss of responsiveness or abnormal movements (possible seizure).

B. Parameter Verification

- Confirm coil placement using:
    - 10–20 EEG system for anatomical localisation.
    - Neuronavigation for precision targeting.

- Check train duration, ITI, and total pulses before starting.

C. Physiological Monitoring

- Standard sessions: Continuous observation is sufficient.
- High-risk patients (neurological history, elderly, comorbidities):
    - BP, HR monitoring.
    - EEG monitoring in research/experimental protocols.

11.4 Post-Session Monitoring

1. Immediate Observation (5–10 min after stimulation):
    - Headache.
    - Lightheadedness.
    - Mood shifts.
    - Visual or auditory disturbances.
2. Documentation:
    - Record stimulation parameters, coil location, patient-reported symptoms.
    - Note any deviations from planned session.
3. Follow-Up Tracking:
    - Review adverse symptoms at next session.
    - Adjust protocol if cumulative discomfort is noted.

11.5 Adverse Effects — Classification & Mechanisms

Category	Example Symptoms	Mechanism	Incidence
Mild, common	Scalp pain, headache, facial twitching	Peripheral nerve/muscle activation	20–40%
Moderate, less common	Fatigue, dizziness, transient mood changes	Cortical excitability modulation, autonomic shifts	5–10%
Serious, rare	Seizure, syncope, hearing loss	Excessive cortical activation, vasovagal reaction, acoustic trauma	<0.1%

11.6 Early Warning Signs

- Seizure prodrome: Sudden blank stare, jerky movements, change in breathing pattern.
- Vasovagal reaction: Pallor, sweating, nausea, hypotension.
- Acoustic discomfort: Ear ringing, muffled hearing.

11.7 Management Protocols

A. Mild Discomfort / Headache

- Pause session; allow rest.
- Offer analgesics (e.g., paracetamol, ibuprofen).
- Adjust coil angle or decrease intensity by 5–10%.

B. Facial Twitching

- Reposition coil slightly to avoid peripheral nerve stimulation.
- Consider lowering train duration or increasing ITI.

C. Dizziness / Fatigue

- Seat patient until stable.
- Encourage hydration.
- Check for postural BP drop.

D. Vasovagal Syncope

- Stop stimulation immediately.
- Recline patient with legs elevated.
- Monitor BP and pulse until recovery.

E. Seizure Management

- Stop stimulation immediately.
- Position patient on their side (recovery position).
- Protect head and airway.
- Call emergency services if seizure lasts >5 minutes or is recurrent.
- Document event fully.

F. Hearing Changes

- Ensure correct ear protection before each session.
- Refer for audiological evaluation if persistent.

11.8 Quality Assurance & Safety Culture

- Maintain an adverse event registry for all patients.
- Conduct quarterly safety audits to track incidents.
- Mandatory annual safety training for all rTMS staff.
- Encourage a no-blame reporting culture to improve protocols.

11.9 Summary Table — Safety & Monitoring Checklist

Stage	Key Actions
Pre-Session	Safety screening, consent, RMT determination, baseline vitals, symptom scoring
Intra-Session	Verify coil position/parameters, monitor for discomfort, track physiological signs
Post-Session	Observe for adverse effects, document findings, plan adjustments if needed

Chapter 12:

Extended Applications & Future Directions

12.1 Introduction

Repetitive Transcranial Magnetic Stimulation (rTMS) offers therapeutic potential beyond its currently approved uses. Its extended applications are grounded in the ability to:

- Modulate cortical excitability — Increasing or decreasing neuronal firing rates through frequency-dependent stimulation.
- Induce neuroplastic changes — Long-term potentiation (LTP) or depression (LTD)-like effects through repeated trains of stimulation.
- Alter neurotransmitter systems — Including glutamatergic, dopaminergic, GABAergic, and endogenous opioid activity.
- Reconfigure network connectivity — By influencing both local circuits and distributed functional networks (e.g., Default Mode Network, Salience Network).
- Shift oscillatory balance — Adjusting spectral power in delta, theta, alpha, beta, and gamma bands to match healthy physiological patterns.

12.2 Condition-Specific Applications and Protocols

12.2.1 Autism Spectrum Disorder (ASD)

Neurophysiological Basis:

- Decreased gamma activity in left hemisphere, increased delta/theta/alpha.
- Disrupted sensory-motor integration and impaired E/I balance.
- Altered functional connectivity between frontal cortex, amygdala, hippocampus, ACC.

Therapeutic Rationale:

- HF-rTMS to left DLPFC enhances executive function and social cognition.
- LF-rTMS to right DLPFC reduces hyperconnectivity and over-excitation.

Reported Outcomes:
Improvement in irritability, repetitive behaviours, attention, social reciprocity, and expressive language.

Site	Mode	PPT	Pulses	Trains	ITI	Sessions	Intensity
F3	HF 5 Hz	10	600	60	8 s	30	100% RMT
F4	LF 1 Hz	30	600	20	2 s	30	100% RMT

12.2.2 Attention-Deficit/Hyperactivity Disorder (ADHD)

Neurophysiology:

- Hypoactivity in right VLPFC/DLPFC and ACC.
- Abnormal alpha–gamma relationship; low theta–gamma coupling.
- Elevated theta and reduced beta over frontal regions; altered coherence patterns.

Therapeutic Rationale:

- Excitatory HF stimulation to underactive right frontal networks improves attention and inhibitory control.
- SMA targeting can reduce hyperactivity via modulation of motor inhibition circuits.

Reported Outcomes:
Improved sustained attention, reduced impulsivity, better response inhibition.

Site	Mode	PPT	Pulses	Trains	ITI	Duration	Intensity
Between F4–F8	HF 18 Hz	36	1440	40	20 s	6 weeks	120% RMT

12.2.3 Mild Cognitive Impairment (MCI) & Alzheimer's Disease (AD)

Neurophysiology:

- Slowing of dominant frequency (alpha → theta/delta).
- Reduced alpha/beta power, increased slow-wave activity.
- Lowered alpha/theta ratio predictive of progression.

Therapeutic Rationale:

- HF-rTMS over DLPFC improves working memory and attention.
- Pz or parietal targets can improve visuospatial and memory functions.

Reported Outcomes:
Better scores on MoCA, ADAS-Cog, verbal fluency, and daily functional performance.

Site	Mode	PPT	Pulses	Trains	ITI	Sessions	Intensity
F3	HF 10 Hz	40	2000	50	26 s	45–60	100% RMT
Pz	HF 20 Hz	40	1600	40	28 s	45–60	100% RMT

12.2.4 Stroke Rehabilitation

Neurophysiology:

- Interhemispheric imbalance: overactivity in contralesional M1, reduced excitability in ipsilesional M1.
- Impaired corticospinal excitability, maladaptive plasticity.

Therapeutic Rationale:

- LF to contralesional M1 reduces transcallosal inhibition.
- HF to ipsilesional M1 facilitates motor output and relearning.

Reported Outcomes:
Improved Fugl-Meyer scores, gait speed, upper limb dexterity, and language recovery in post-stroke aphasia.

Site	Mode	Pulses	Sessions	Intensity
Contralesional M1	LF 1 Hz	1000 pulses	15	100% RMT
Ipsilesional M1	HF 10 Hz	1000–1350 pulses	15	90–100% RMT

12.2.5 Tinnitus

Neurophysiology:

- Overactivation in auditory cortex and temporo-parietal networks.

Therapeutic Rationale:

- LF suppression reduces hyperexcitability and tinnitus loudness.

Site	Mode	Pulses	Sessions	Intensity
Contralateral TPJ	LF 1 Hz	1200–2000	5–10	90–100% RMT

12.2.6 Schizophrenia

Neurophysiology:

- Reduced gamma oscillations, altered hemispheric power distribution.
- Left TPJ hyperactivity associated with auditory hallucinations; DLPFC hypoactivity linked to negative symptoms.

Therapeutic Rationale:

- LF TPJ stimulation decreases hallucination severity.
- HF DLPFC stimulation improves motivation and affect.

Site	Mode	Pulses	Sessions	Intensity
Left TPJ	LF 1 Hz	300–1000	10–12	90% RMT
Left DLPFC	HF 10 Hz	1000–2000	10–15	100% RMT

12.2.7 Substance Use Disorders

Neurophysiology:

- Dysregulation in prefrontal–striatal reward circuits; frontal alpha asymmetry.

Therapeutic Rationale:

- HF DLPFC stimulation reduces craving, modulates dopamine release, and improves executive control.

Site	Mode	Pulses	Sessions	Intensity
Right DLPFC	HF 10–15 Hz	2000–3000	20–30	100–120% RMT

12.2.8 Migraine

Neurophysiology:

- Cortical spreading depolarisation implicated in migraine aura.

Therapeutic Rationale:

- Disrupting depolarisation waves via patterned HF vertex stimulation.

Protocol: Patterned HF stimulation over vertex, twice weekly for 3 weeks.

12.2.9 Parkinson's Disease

Neurophysiology:

- Hypoactivity in SMA and M1; impaired basal ganglia–cortical communication.

Therapeutic Rationale:

- SMA stimulation improves bradykinesia, gait, and motor initiation.

Site	Mode	PPT	Pulses	Sessions	Intensity
SMA	HF 10 Hz	5	1000	10	100% RMT

12.2.10 Pain Syndromes / Fibromyalgia

Neurophysiology:

- Hyperactivity in pain matrix regions; altered thalamo-cortical rhythms.

Therapeutic Rationale:

- HF M1 stimulation reduces central sensitization and pain intensity.

Site	Mode	Pulses	Sessions	Intensity
C3	HF 10 Hz	1500	15	90% RMT

12.2.11 Tourette's Syndrome

Neurophysiology:

- Dysregulated SMA–basal ganglia circuits; excessive motor drive.

Therapeutic Rationale:

- LF SMA stimulation reduces tic frequency and severity.

Site	Mode	Pulses	Sessions	Intensity
SMA	LF 1 Hz	1200	10	100% RMT

12.3 Future Directions

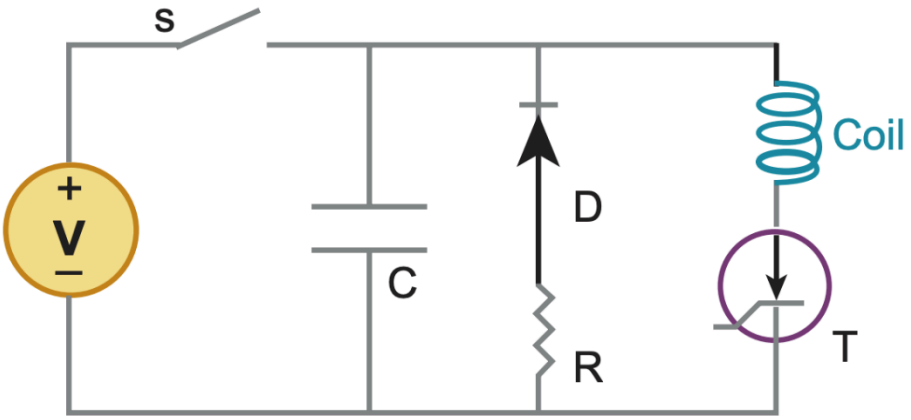
- QEEG-guided and Connectome-based Targeting: Individualised mapping of stimulation sites using functional connectivity analysis.
- Closed-loop rTMS: Real-time EEG feedback to adjust stimulation parameters dynamically.
- Combination Therapies: Integrating rTMS with cognitive training, physiotherapy, psychotherapy, or pharmacological modulation.
- Portable/Home-based Devices: For maintenance therapy in chronic conditions under remote supervision.
- Emerging Indications: PTSD subtypes, eating disorders, traumatic brain injury, neurodevelopmental disorders, and cognitive enhancement in ageing.

Disclaimer:
Many of the indications discussed here are *off-label* for rTMS. While there is growing evidence for their efficacy, their use should be restricted to specialist clinical or research settings, delivered by trained professionals following consensus safety guidelines. Protocol parameters are derived from peer-reviewed literature and should be tailored to the individual patient's neurophysiology, comorbidities, and tolerance.

Appendix :

- *Pulse-shape circuitry*

  Specialized circuitry can be used to generate either monophasic or biphasic pulses



(*V* voltage source, *S* switch, *C* capacitor, *D* diode, *R* resistor, *T* thyristor)

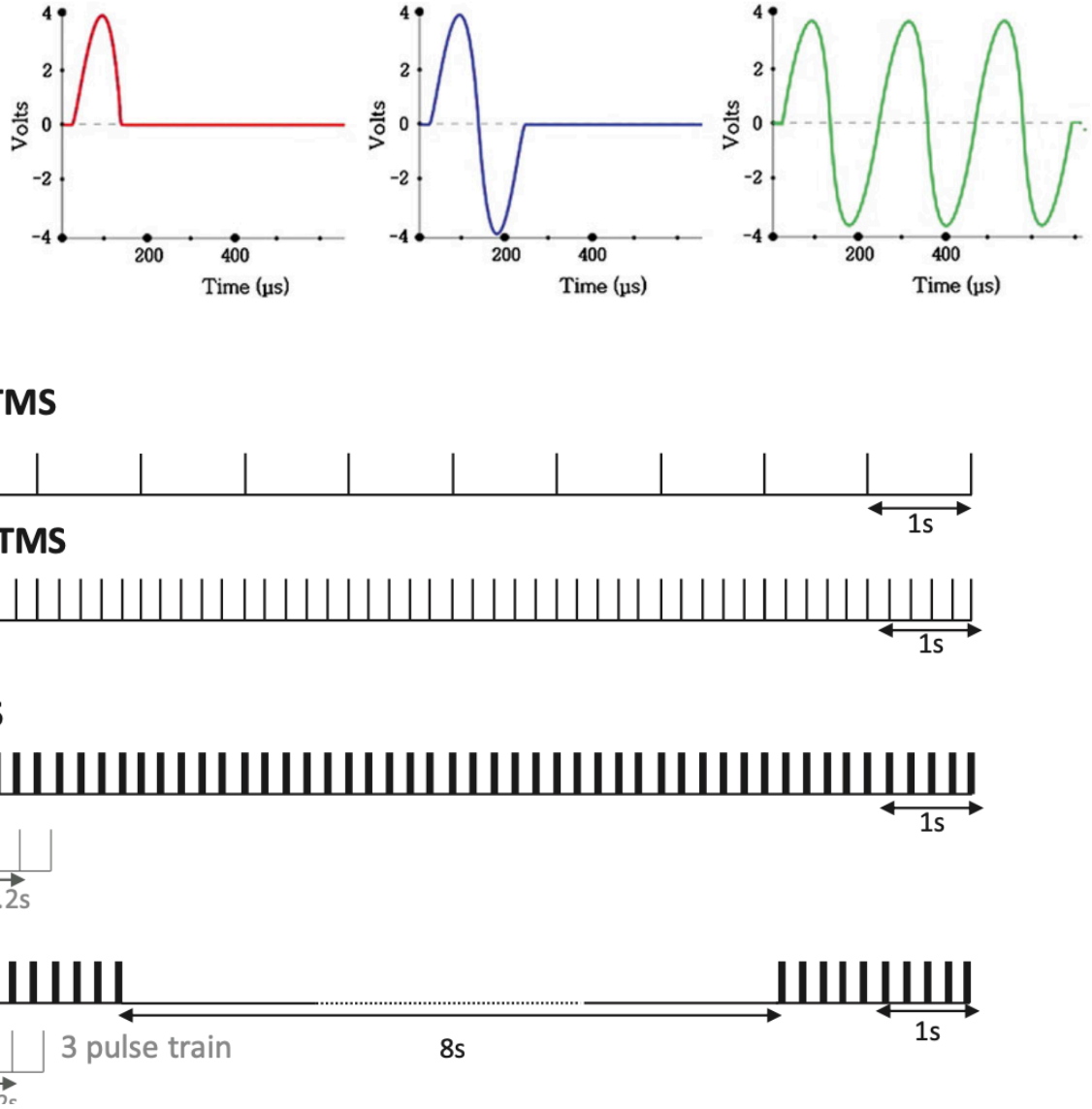
- Stimulating Coil

Round Coil, Figure-of-Eight Coil, Double Coil, H-Coil

Pulse Waveforms

Monophasic

Biphasic/Polyphasic

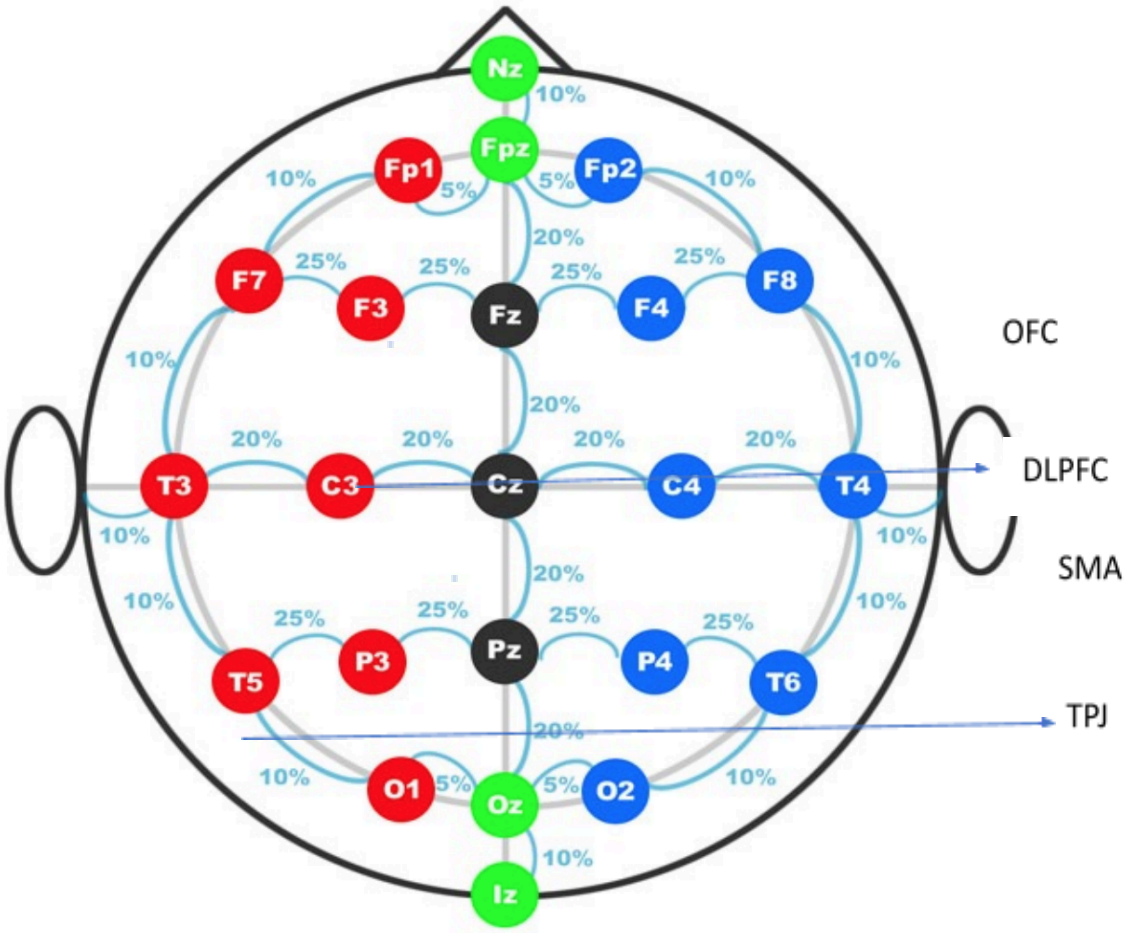


Simple repetitive TMS (rTMS) protocols consist of identical stimuli spaced by an identical inter-stimulus interval (ISI). Effects depend on stimulation frequency: at low frequency (LF rTMS < 1 Hz), rTMS depresses excitability in the motor cortex, whereas at high frequency (HF rTMS > 5 Hz), cortical excitability is increased. Theta burst stimulation (TBS) involves bursts of high-frequency stimulation (3 pulses at 50 Hz) repeated with an ISI of 200 ms (5 Hz). In an intermittent TBS (iTBS) protocol, bursts are delivered for 2 s, then repeated every 10 s (2 s of TBS followed by a pause of 8 s). However, in a continuous TBS protocol (cTBS), bursts are repeated for 40 s without any pause.

10 -20 System

An internationally recognised method that allows EEG electrode placement to be standardised. Ensures inter-electrode spacing is equal, Electrode placements proportional to skull size & shape
Covers all brain regions

F = Frontal T = Temporal P = Parietal O = Occipital • Numbering system



Orbitofrontal Cortex (OFC) - Fp1
DorsolateralPrefrontal Cortex (DLPFC)- F3
Supplementary Motor Area (SMA) -
Temporo Parietal Junction (TPJ)

Locating C3 :
Nasion to Inion Distance :
Inter Pre-Auricular Distance :
Intersection is CZ:
20% on the left side along the line: C3

1. Orbitofrontal Cortex (OFC) – Fp1

- 10–20 Location: Fp1 (left frontopolar)
- Position: Most anterior left frontal electrode, just above the left eyebrow, near midline.
- Underlying cortical area: Left medial and lateral orbitofrontal cortex.
- Functions: Emotional regulation, reward valuation, social decision-making.
- rTMS note: Accessed in certain obsessive-compulsive disorder (OCD) and addiction protocols; coil is often tilted to target more ventrally.

2. Dorsolateral Prefrontal Cortex (DLPFC) – F3

- 10–20 Location: F3 (left mid-lateral frontal electrode).
- Position: Lateral to Fz, anterior to C3.
- Underlying cortical area: Left middle frontal gyrus (Brodmann areas 9/46).
- Functions: Executive function, working memory, top-down control of emotion.
- rTMS note: High-frequency stimulation here is standard for major depressive disorder.

3. Supplementary Motor Area (SMA)

- 10–20 Location: Roughly midway between Fz and Cz on the midline.
- Position: Medial frontal cortex, anterior to the primary motor cortex.
- Underlying cortical area: Medial superior frontal gyrus, including pre-SMA and SMA-proper.
- Functions: Motor planning, initiation, bimanual coordination.
- rTMS note: Midline targeting; implicated in protocols for Parkinson's disease, Tourette's, and compulsive disorders.

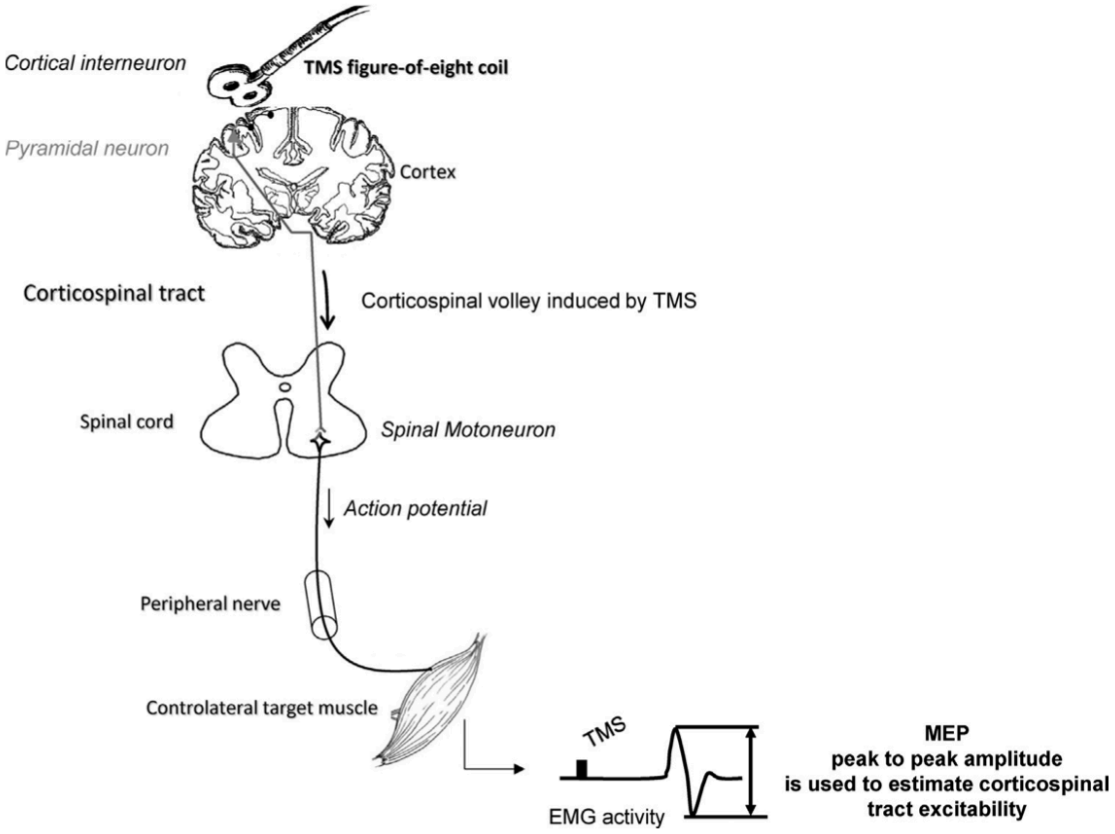
4. Temporoparietal Junction (TPJ)

- 10–20 Location: Near CP5 (left TPJ) or CP6 (right TPJ).
    - Some use P5/P6 or between T3 (T7) and P3 (for left TPJ).
- Position: Posterior to the superior temporal gyrus, inferior to the inferior parietal lobule.

- Underlying cortical area: Angular gyrus + posterior superior temporal sulcus.
- Functions: Social cognition, theory of mind, multisensory integration, language.
- rTMS note: Left TPJ stimulation is used for auditory hallucinations in schizophrenia; right TPJ for studies on social processing.

MEP:

Motoneuron activation in response to corticospinal volleys induced by TMS leads to a contraction in the target muscle evoking a motor-evoked potential (MEP) on electromyography (EMG) recorded by using surface electrodes applied over the muscle belly. Its peak-to-peak amplitude is used to estimate excitability of the corticospinal tract.



The motor threshold is measured at the individual motor hotspot—the scalp site over M1 hand area yielding the largest, most reliable APB/FDI MEPs—defined as the lowest output evoking ≥50 μV MEPs in ≥5/10 trials (RMT) with the coil tangential, ~45° for PA current, under standardized EMG and coil-geometry conditions.

A standard screening questionnaire for rTMS candidates (Rossi et al 2009)

Investigators should consider using a standard questionnaire to screen rTMS candidates. The following questions represent the basic information required. Additional information may change according to particular demands. Consensus has been reached for this questionnaire.

1. Do you have epilepsy or have you ever had a convulsion or a seizure? Yes ( ) / No ( )
2. Have you ever had a fainting spell or syncope? Yes ( ) / No ( )

   If yes, please describe in which occasion(s)

3. Have you ever had severe (i.e., followed by loss of consciousness) head trauma? Yes ( ) / No ( )
4. Do you have any hearing problems or ringing in your ears? Yes ( ) / No ( )
5. Are you pregnant or is there any chance that you might be? Yes ( ) / No ( )
6. Do you have metal in the brain/skull (except titanium)? (e.g., splinters, fragments, clips, etc.) Yes ( ) / No ( )
7. Do you have cochlear implants? Yes ( ) / No ( )
8. Do you have an implanted neurostimulator (e.g., DBS, epidural/subdural)? Yes ( ) / No ( )
9. Do you have a cardiac pacemaker or intracardiac lines or metal in your body? Yes ( ) / No ( )
10. Do you have a medication infusion device? Yes ( ) / No ( )
11. Are you taking any medications? Yes ( ) / No ( )

    If yes, please note the name and dosage of all medications

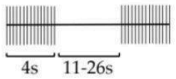
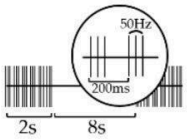
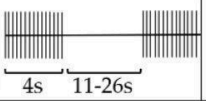
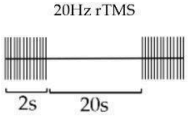
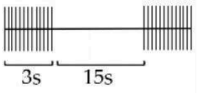
12. Did you ever have a surgical procedures to your spinal cord? Yes ( ) / No ( )
13. Do you have spinal or ventricular derivations? Yes ( ) / No ( )
14. Did you ever undergo TMS in the past? Yes ( ) / No ( )
15. Did you ever undergo MRI in the past? Yes ( ) / No ( )

Affirmative answers to one or more of questions 1–13 do not represent absolute contraindications to TMS, but the risk/benefit ratio should be carefully balanced by the Principal Investigator of the research project or by the responsible (treating) physician.

Location	Underlying Cortical Region	Primary Functional Association
Fp1	Left prefrontal cortex (superior/middle frontal gyrus)	Executive functions, working memory, emotional regulation
Fp2	Right prefrontal cortex (superior/middle frontal gyrus)	Attention, emotional regulation
F3	Left dorsolateral prefrontal cortex (DLPFC)	Cognitive control, mood regulation (common rTMS target in depression)
F4	Right dorsolateral prefrontal cortex (DLPFC)	Attention, working memory
F7	Left inferior frontal gyrus (Broca's area region)	Speech production, language
F8	Right inferior frontal gyrus	Response inhibition, emotional regulation
C3	Left primary motor cortex (precentral gyrus)	Voluntary motor control (right body)
C4	Right primary motor cortex (precentral gyrus)	Voluntary motor control (left body)
P3	Left posterior parietal cortex	Spatial attention, sensory integration
P4	Right posterior parietal cortex	Spatial awareness, visuospatial processing
O1	Left occipital cortex	Visual processing (right visual field)
O2	Right occipital cortex	Visual processing (left visual field)
T3/T7	Left superior temporal gyrus	Auditory processing, language comprehension
T4/T8	Right superior temporal gyrus	Auditory processing, prosody, social cues
Fz	Midline prefrontal cortex	Cognitive control, decision-making
Cz	Midline central cortex	Motor coordination, bilateral movement

Pz	Midline parietal cortex	Sensory integration, attention shifts
Oz	Midline occipital cortex	Central visual field processing

Table 1. Description of FDA-cleared transcranial magnetic stimulation protocols to treat psychiatric disorders.

Disorder	Frequency	Ses. Pulses (Duration)	Schedule (No Ses.)	Target Region	Examples of TMS Manufacturers (Coils)
Major Depressive Episode	10Hz rTMS 	3000 (18′ 48″ to 37′ 30″)	1/d (20–30d)	L-DLPFC	NeuroStar 
				L-DLPFC	Magstim (e.g., HORIZON® Coils) 
				BL-DLPFC (L-DLPFC)	Brainsway (H1 coil) 
				L-DLPFC	Magventure (e.g., B65 coil) 
	Intermittent Theta Burst 	600 (3′ 9″)	1/d (20–30 d)	L-DLPFC	NeuroStar  Magstim  Magventure 
		18000 (9′ 27″)	Accelerated: 10/d (5 d)	L-DLPFC	Magventure (B65 coil) 
With Comorbid Anxiety	20Hz rTMS 	1980 (20′ 12″)	1st: 1/d (20 d) 2nd: 2/w (12 w)	BL-DLPFC (L-DLPFC)	Brainsway (H1 coil) 
	10Hz rTMS 	3000 (18′ 48″)	1st: 1/d (30 d) 2nd: ~2/w (3 w)	L-DLPFC	NeuroStar 
Obsessive Compulsive Disorder	20Hz rTMS 	2000 (18′)	1/day (29 d)	ACC/mPFC	Brainsway (H7 coil) 
				ACC/mPFC	Magventure (DB-80 coil) 
Smoking Cessation	10Hz rTMS 	1800 (17′ 48″)	1st: 1/d (15d) 2nd: 1/w (3 w)	BL-lPFC BL-Insula	Brainsway (H4 coil) 

′—minutes; ″—seconds; ACC—anterior cingulate cortex; BL—bilateral; CE—Conformitè Europëenne; d—day; DLPFC—dorsolateral prefrontal cortex; FDA—Food and Drug Administration; Hz—Hertz; L—left; lPFC—lateral

Table 2. Summary of recommendations of TMS in psychiatric disorders.

Major Depressive Episode	Definite antidepressant effect of HF-TMS of the left DLPFC (Level A)
	Probable antidepressant effect of LF-TMS of the right DLPFC (Level B) and probably no differential antidepressant effect between right LF-TMS and left HF-TMS (Level B)
	Definite antidepressant effect of rTMS of the DLPFC in unipolar depression (Level A), but no recommendation for bipolar depression
	Antidepressant effect of rTMS of the DLPFC is probably additive to the efficacy of antidepressant drugs (Level B) and possibly potentiating (Level C)
PTSD	Possible effect of HF-TMS of the right DLPFC (Level C)
Auditory hallucinations	Possible effect of LF-TMS of the left TPC (Level C)
Negative symptoms of schizophrenia	Probable effect of HF-TMS of the left DLPFC (Level B)
Addiction and craving	Possible effect of HF-rTMS of the left DLPFC on cigarette craving and consumption (Level C)

HF—high-frequency; LF—low-frequency; TMS—transcranial magnetic stimulation; DLPFC—dorsolateral prefrontal cortex; TPC—temporoparietal cortex; PTSD—post-traumatic stress disorder. Level A ("definitely effective or ineffective") required at least two Class I studies or one Class I study and at least two Class II studies; Level B ("probably effective or ineffective") required at least two Class II studies or the combination of one Class I or II study and at least two Class III studies; and Level C ("possibly effective or ineffective") required at least two Class III studies or any combination of two studies of different Classes I, II, or III. Table adapted from Lefaucheur, J.P. et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clin. Neurophysiol.* **2014**, *125*, 2150–2206 [59].

Source : Cotovio, G.; Ventura, F.; Rodrigues da Silva, D.; Pereira, P.; Oliveira-Maia, A.J. Regulatory Clearance and Approval of Therapeutic Protocols of Transcranial Magnetic Stimulation for Psychiatric Disorders. Brain Sci. 2023, 13, 1029. https://doi.org/10.3390/brainsci13071029

Suggested Reading

1. Safety & Foundational Guidelines

- Rossi S, Hallett M, Rossini PM, Pascual-Leone A. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, 120(12), 2008–2039.
  https://pubmed.ncbi.nlm.nih.gov/19833552/

- Rossi S, et al. (2021). Updated safety guidelines for TMS use in healthy subjects and patients, including seizure risk and operational standards. *Clinical Neurophysiology*, 132(1), 269–306.
  https://pubmed.ncbi.nlm.nih.gov/33243615/

2. FDA Protocols & Device Approvals

- U.S. Food and Drug Administration (2011). Class II Special Controls Guidance for Repetitive Transcranial Magnetic Stimulation (rTMS) Systems.

  https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/repetitive-transcranial-magnetic-stimulation-rtms-systems-class-ii-special-controls-guidance

- Trapp NT, et al. (2024). Advances in rTMS protocols including FDA-cleared intermittent theta-burst stimulation (iTBS). *Seizure*, 105, 53–64.
  https://www.sciencedirect.com/science/article/pii/S1388245724003766

- BlueCross NC (2013). FDA clearance of Deep TMS for treatment-resistant depression.

  https://www.bluecrossnc.com/providers/policies-guidelines-codes/commercial/behavioral-health/updates/transcranial-magnetic-stimulation-tms

3. Consensus Recommendations & Clinical Evidence

- McClintock SM, et al. (2018). Consensus recommendations for the clinical application of rTMS in depression. *Journal of Clinical Psychiatry*, 79(1).
  https://pmc.ncbi.nlm.nih.gov/articles/PMC5846193/

- Perera MPN, et al. (2021). Meta-analysis of rTMS for obsessive-compulsive disorder. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*.

  https://www.researchgate.net/publication/367538044_Clinical_practice_guidelines_for_the_therapeutic_use_of_repetitive_transcranial_magnetic_stimulation_in_neuropsychiatric_disorders

4. Indian Psychiatric Society (IPS) Clinical Practice Guidelines

- Tikka SK, et al. (2023). IPS-CPG for the therapeutic use of rTMS in psychiatric disorders. *Indian Journal of Psychiatry*, 65(Suppl 1), S1–S55.
  https://pmc.ncbi.nlm.nih.gov/articles/PMC10096206/

- IPS (2017). Clinical practice guidelines for the management of depression, OCD, and other disorders including rTMS recommendations.

  https://indianpsychiatricsociety.org/wp-content/uploads/2017/01/Gautam_2017_Clinical_Practice_Guidelines_for_the.pdf

5. Reviews & Overviews

- Hallett M. (2007). Transcranial magnetic stimulation: A primer. *Neuron*, 55(2), 187–199.
  https://doi.org/10.1016/j.neuron.2007.06.026

- Cotovio G, et al. (2023). Regulatory clearance and approval of therapeutic protocols of TMS for psychiatric disorders. *Frontiers in Psychiatry*, 14, 111111.
  https://pmc.ncbi.nlm.nih.gov/articles/PMC10377201/

6. Applications Beyond Depression

- Heidarpanah A, et al. (2022). Non-invasive brain stimulation in Alzheimer's disease: rTMS and tDCS applications. *Frontiers in Aging Neuroscience*, 14, 993306.
  https://doi.org/10.3389/fnagi.2022.993306

- Saitoh Y, et al. (2022). Safety and feasibility of rTMS in mild-to-moderate Alzheimer's disease. *Frontiers in Aging Neuroscience*, 14, 993306.
  https://doi.org/10.3389/fnagi.2022.993306

7. Books & Texts

- George MS, Belmaker RH (Eds.). (2000). *Transcranial Magnetic Stimulation in Neuropsychiatry*. American Psychiatric Press.
  https://doi.org/10.1176/appi.books.9781585626463

- Diefenbach GJ, et al. (2022). *rTMS Treatment for Depression: A Practical Guide*. Springer.
  https://doi.org/10.1007/978-3-030-91519-9

- Robison JE. (2016). *Switched On: A Memoir of Brain Change and Emotional Awakening*. Spiegel & Grau.
  https://www.penguinrandomhouse.com/books/317169/switched-on-by-john-elder-robison/

Disclaimer

This handbook is intended for educational purposes for participants of the *rTMS 360° – National Conference & Hands-On Workshop*. The content is compiled from publicly available literature, expert contributions, and consensus guidelines, and is **not** a substitute for formal training or clinical judgment. Protocols described herein should be applied only by trained professionals in appropriate clinical settings.

While every effort has been made to ensure accuracy and currency of information, the authors and organizers do not accept responsibility for any errors, omissions, or consequences arising from its use. Readers are encouraged to verify details from primary sources before implementation.

For corrections, suggestions, or feedback, please contact: **srinivasaiims@gmail.com**

This book is intended for educational purposes only and should **not** be construed as medical advice. Medical knowledge and evidence evolve continuously, and new research, updated clinical guidelines, and emerging treatments may change recommendations at any time. Readers are strongly advised to consult current, reputable sources and relevant clinical guidelines, and to seek the advice of qualified healthcare professionals before making decisions related to patient care.

The authors and publishers disclaim any liability for the consequences of applying the information in this book without proper professional judgment and up-to-date verification.