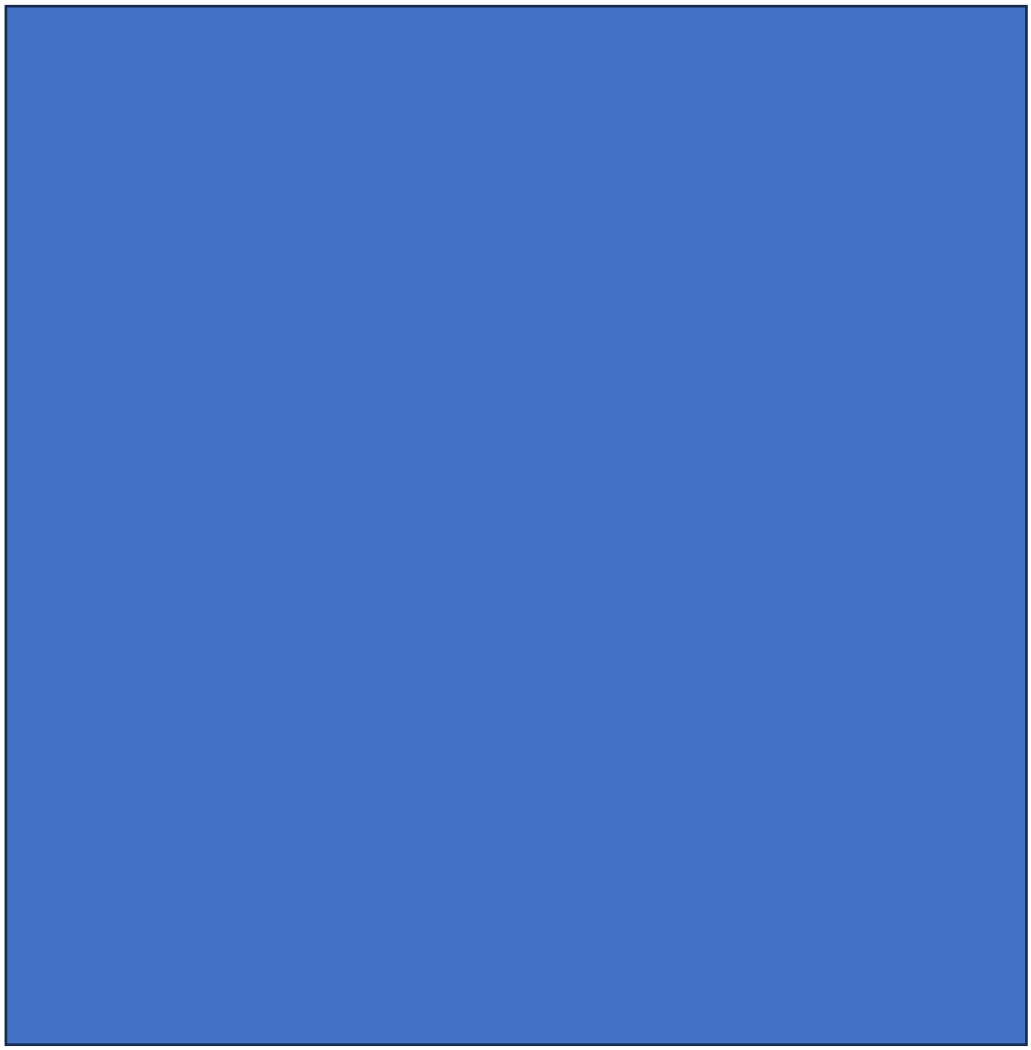
“KETAMINE VERSUS ELECTROCONVULSIVE THERAPY FOR MAJOR DEPRESSIVE DISORDER: A RANDOMIZED CONTROLLED COMPARATIVE STUDY.”



NAME OF COURSE	**M.D. PSYCHIATRY**
NAME OF SUBJECT	**PSYCHIATRY**
ADMISSION YEAR / ACADEMIC YEAR	**2022/2022-2025**

LIST OF ABBREVIATIONS

- MDD -Major Depressive Disorder
- TRD -Treatment-Resistant Depression
- ECT -Electroconvulsive Therapy
- NMDA -N-Methyl-D-Aspartate
- HAM-D -Hamilton Depression Rating Scale
- MADRS -Montgomery–Åsberg Depression Rating Scale
- MSSI - Modified Scale for Suicidal Ideation
- MINI - Mini International Neuropsychiatric Interview
- BDI- Beck Depression Inventory
- BDNF- Brain-Derived Neurotrophic Factor
- HPA - Hypothalamic–Pituitary–Adrenal Axis
- mTOR - Mammalian Target of Rapamycin
- IL-6 - Interleukin-6
- TNF-α - Tumor Necrosis Factor-alpha
- CRP - C-Reactive Protein
- SSRIs - Selective Serotonin Reuptake Inhibitors
- SNRIs - Serotonin-Norepinephrine Reuptake Inhibitors
- TCAs - Tricyclic Antidepressants
- MAOIs - Monoamine Oxidase Inhibitors
- rTMS - Repetitive Transcranial Magnetic Stimulation

- VNS - Vagus Nerve Stimulation
- DBS - Deep Brain Stimulation
- tDCS - Transcranial Direct Current Stimulation
- APA - American Psychiatric Association
- DSM-5 - Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
- ICD-11 - International Classification of Diseases, 11th Revision
- WHO - World Health Organization
- DLPFC - Dorsolateral Prefrontal Cortex

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INTRODUCTION

INTRODUCTION

Major Depressive Disorder (MDD) is a globally prevalent psychiatric condition, representing a significant public health burden due to its high prevalence, chronic nature, and substantial impairment in social and occupational functioning (1). According to the World Health Organization (WHO), depression is the leading cause of disability worldwide and is a major contributor to the overall global burden of disease. [redacted]

[redacted] Despite its proven efficacy, the use of ECT is often limited by its invasiveness, associated cognitive side effects, stigma, and the requirement for anaesthesia and hospital-based infrastructure (4). [redacted]

In recent years, ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist traditionally used as an anaesthetic agent, has emerged as a promising rapid-acting antidepressant, especially in patients with TRD (5). [redacted]

The comparison between ketamine and ECT in the treatment of MDD is of increasing clinical interest.

Several studies have attempted to compare the efficacy, onset of action, and safety of ECT and ketamine in depression.

[redacted]

[redacted]The study also intends to address the feasibility of using oral ketamine as a less invasive, cost-effective alternative to ECT in specific subsets of patients.

AIMS AND OBJECTIVE

AIM AND OBJECTIVES

AIM:

[redacted]

OBJECTIVE:

[redacted]

REVIEW OF LITERATURE

REVIEW OF LITERATURE

WHO Definition of Depression

According to the World Health Organization (WHO):

"A common mental disorder characterized by persistent sadness and a lack of interest or pleasure in previously rewarding or enjoyable activities. [redacted]

It is a serious medical illness that needs timely recognition and treatment (20).

Classification of Depression (DSM-5)

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), published by the American Psychiatric Association (APA), classifies depression under the broader category of "Depressive Disorders." [redacted]

Classification of depressive disorders	
Depressive disorders in the DSM-5	Depressive disorders in the ICD-11
Disruptive mood dysregulation disorder	Single episode depressive disorder
Major depressive disorder	Recurrent depressive disorder
Persistent depressive disorder (dysthymia)	Dysthymic disorder
Premenstrual dysphoric disorder	Mixed depression and anxiety disorder
Substance/medication-induced depressive disorder	Premenstrual dysphoric disorder
Depressive disorder due to another medical condition	Other specified depressive disorders
Unspecified depressive disorder	Depressive disorders, unspecified
Specifiers for depressive disorders	Other specified mood disorders
	Mood disorders, unspecified specification

Fig 1 Depressive disorders according to DSM-5 and ICD- 11. 10,11(22)

Main Subtypes of Depressive Disorders in DSM-5:

1. **Major Depressive Disorder (MDD)**

[redacted]

Diagnostic Criteria: [redacted]

[redacted]

2. **Persistent Depressive Disorder (Dysthymia)**

- Chronic, low-grade depression lasting for at least 2 years in adults (1 year in children/adolescents) (23).

[redacted]

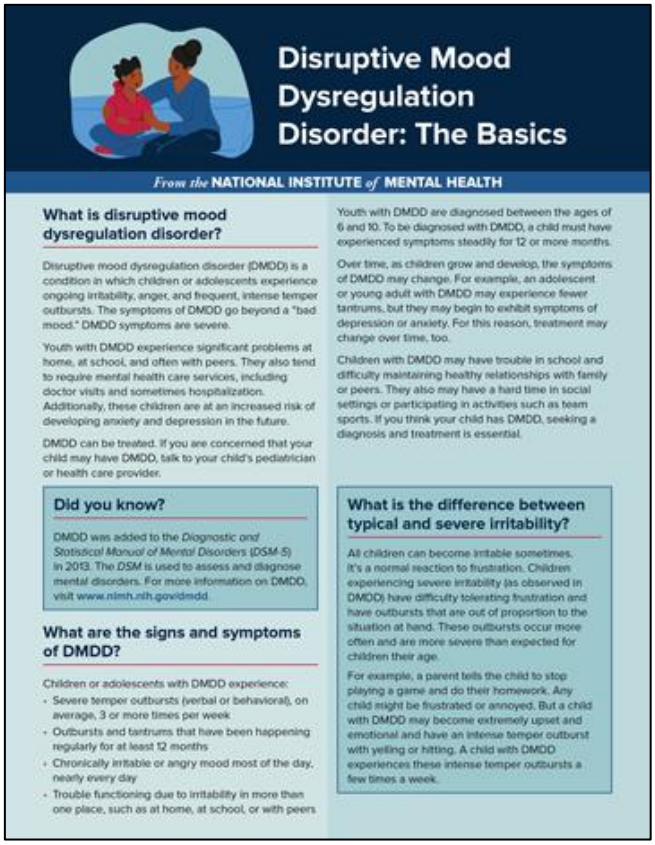
[redacted]

6. Feelings of hopelessness

3. **Disruptive Mood Dysregulation Disorder (DMDD)**

- Diagnosed in children aged 6 to 18 years.

[redacted]



Disruptive Mood Dysregulation Disorder: The Basics

From the NATIONAL INSTITUTE *of* MENTAL HEALTH

What is disruptive mood dysregulation disorder?

Disruptive mood dysregulation disorder (DMDD) is a condition in which children or adolescents experience ongoing irritability, anger, and frequent, intense temper outbursts. The symptoms of DMDD go beyond a "bad mood." DMDD symptoms are severe.

Youth with DMDD experience significant problems at home, at school, and often with peers. They also tend to require mental health care services, including doctor visits and sometimes hospitalization. Additionally, these children are at an increased risk of developing anxiety and depression in the future.

DMDD can be treated. If you are concerned that your child may have DMDD, talk to your child's pediatrician or health care provider.

Did you know?

DMDD was added to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*) in 2013. The *DSM* is used to assess and diagnose mental disorders. For more information on DMDD, visit www.nimh.nih.gov/dmdd.

What are the signs and symptoms of DMDD?

Children or adolescents with DMDD experience:

- Severe temper outbursts (verbal or behavioral), on average, 3 or more times per week
- Outbursts and tantrums that have been happening regularly for at least 12 months
- Chronically irritable or angry mood most of the day, nearly every day
- Trouble functioning due to irritability in more than one place, such as at home, at school, or with peers

Youth with DMDD are diagnosed between the ages of 6 and 10. To be diagnosed with DMDD, a child must have experienced symptoms steadily for 12 or more months.

Over time, as children grow and develop, the symptoms of DMDD may change. For example, an adolescent or young adult with DMDD may experience fewer tantrums, but they may begin to exhibit symptoms of depression or anxiety. For this reason, treatment may change over time, too.

Children with DMDD may have trouble in school and difficulty maintaining healthy relationships with family or peers. They also may have a hard time in social settings or participating in activities such as team sports. If you think your child has DMDD, seeking a diagnosis and treatment is essential.

What is the difference between typical and severe irritability?

All children can become irritable sometimes. It's a normal reaction to frustration. Children experiencing severe irritability (as observed in DMDD) have difficulty tolerating frustration and have outbursts that are out of proportion to the situation at hand. These outbursts occur more often and are more severe than expected for children their age.

For example, a parent tells the child to stop playing a game and do their homework. Any child might be frustrated or annoyed. But a child with DMDD may become extremely upset and emotional and have an intense temper outburst with yelling or hitting. A child with DMDD experiences these intense temper outbursts a few times a week.

Fig 2 Disruptive Mood Dysregulation Disorder: The Basics (24)

4. **Premenstrual Dysphoric Disorder (PMDD)**

[redacted]

[redacted]

5. **Substance/Medication-Induced Depressive Disorder**

[redacted]

6. **Depressive Disorder Due to Another Medical Condition**

[redacted]

7. **Other Specified or Unspecified Depressive Disorder**

[redacted]

Specifiers for Major Depressive Disorder (DSM-5):

[redacted]

- With catatonia

ICD-11 Classification of Depression

[redacted]

Depressive disorders."

The two main diagnostic codes are:

- **6A70 – Single Episode Depressive Disorder**

  [redacted]

- **6A71 – Recurrent Depressive Disorder**

  [redacted]

Each episode can be categorized into:

- Mild depressive episode

[redacted]

ICD-11 Criteria Highlights:

- Symptoms must persist for at least 2 weeks.

[redacted]

[redacted]

- The diagnosis is based on clinical assessment; there are no definitive laboratory markers.

Epidemiology of Major Depressive Disorder (MDD)

Global Epidemiology

Major Depressive Disorder (MDD) is a highly prevalent mental health condition worldwide and is a leading contributor to the global burden of disease.

[redacted]

In many low- and middle-income countries, more than 75% of individuals with depression do not receive appropriate care due to stigma, lack of trained professionals, and limited mental health infrastructure.

Epidemiology in India

India bears a significant share of the global burden of depression. [redacted]

The Indian government has made strides through programs like the District Mental Health Programme (DMHP) and the National Mental Health Programme (NMHP), but accessibility and integration into primary care remain limited (16).

Epidemiology in Maharashtra

Maharashtra, being one of the most urbanized and populous states in India, shows a comparable or slightly higher burden of depressive disorders than the national average. [redacted]

[redacted]

- In Maharashtra, the current prevalence is around 2.9%, with higher burdens in urban centers and underdiagnosis in rural areas (19).

Etiology and Risk Factors of Major Depressive Disorder

Major Depressive Disorder (MDD) is a multifactorial psychiatric condition with a complex interplay of biological, psychological, and environmental components. [redacted]

Table 1 Key Risk Factors for Major Depressive Disorder (MDD)

Category	Key Risk Factors
Biological	[redacted]
Psychological	[redacted]
Environmental	[redacted]
Comorbidities	[redacted]

Pathophysiology of MDD

The pathophysiology of Major Depressive Disorder (MDD) is complex and multifactorial, involving alterations in neurochemistry, brain structure and function, endocrine signaling, immune activation, and neuroplasticity. [redacted]

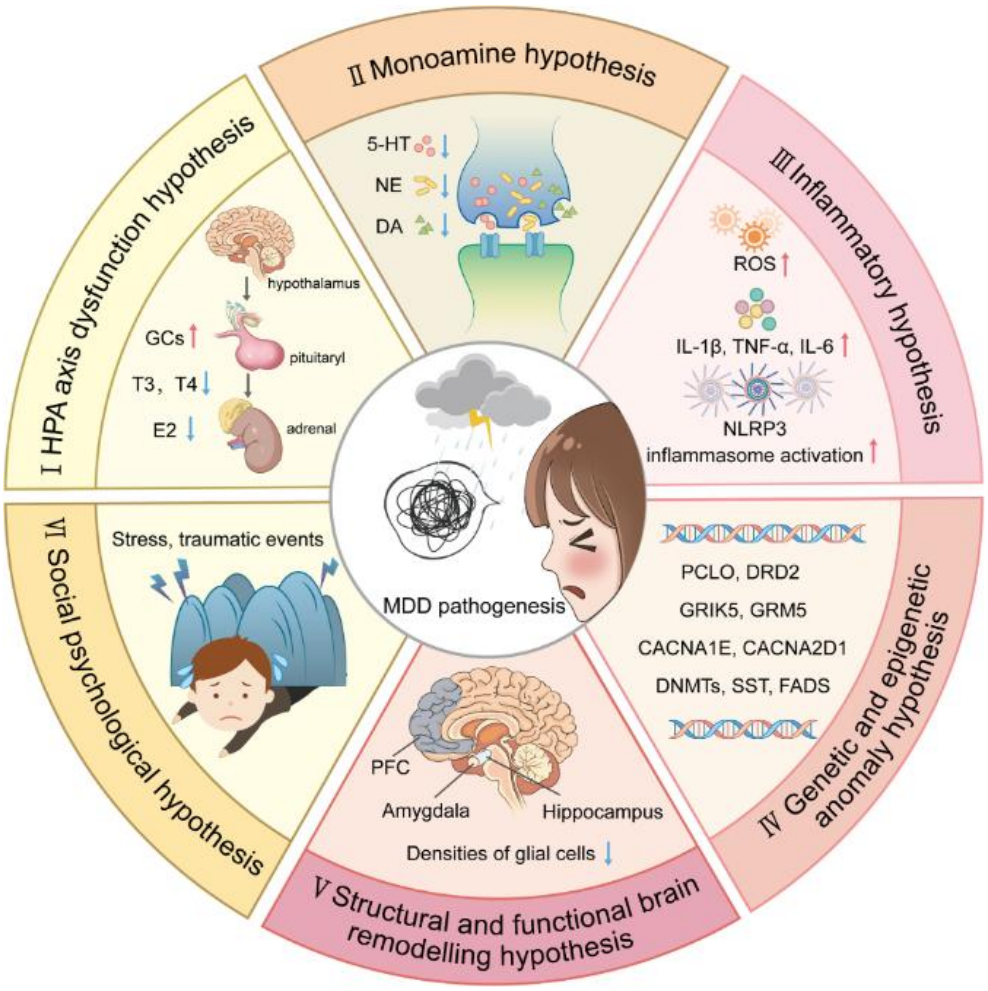


Fig 3 An outline map of the hypotheses to explain MDD pathogenesis. (29)

1. Neurotransmitter Imbalance – The Monoamine Hypothesis

[redacted]

- **Serotonin (5-HT)** – [redacted]
- **Norepinephrine (NE)** – [redacted]
- **Dopamine (DA)** – [redacted]

[redacted]

2. Hypothalamic-Pituitary-Adrenal (HPA) Axis Dysregulation

The HPA axis governs the body's response to stress. [redacted]

- [redacted]
- [redacted]
- [redacted]

The excessive stress response contributes to sleep disruption, cognitive deficits, and anxiety, frequently coexisting with depression.

3. Neuroplasticity and Brain-Derived Neurotrophic Factor (BDNF)

BDNF is a crucial protein involved in neuronal survival, growth, and synaptic plasticity.

- Patients with MDD have reduced levels of BDNF, especially in the hippocampus and prefrontal cortex.

[redacted]

4. Functional and Structural Brain Changes

Neuroimaging studies (fMRI, PET, MRI) in depressed individuals have shown:

- **Decreased volume** and activity in:

  [redacted]

- **Increased activity** in:

  - Amygdala (fear and emotional processing)

    [redacted]

[redacted]

5. Glutamatergic Dysregulation and NMDA Receptors

Emerging research highlights the role of glutamate, the brain's primary excitatory neurotransmitter:

[redacted]

This theory has shifted attention beyond monoamines, providing new therapeutic targets.

6. Inflammation and Immune Activation

Many studies now suggest that MDD is associated with low-grade systemic inflammation:

[redacted]

- Inflammatory activation may also predict treatment resistance in some patients.

7. Gut-Brain Axis and Microbiota

Recent research suggests an important role of the gut microbiome in modulating brain function and mood:

[redacted]

- Probiotics and diet-based interventions are being explored as adjunct treatments in depression.

Table 2 Summary of Key Pathophysiological Mechanisms

Mechanism	Pathological Feature
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Clinical Features and Diagnostic Criteria of Major Depressive Disorder (MDD)

[redacted]

[redacted]

[redacted]

A. Clinical Features

The hallmark features of MDD include:

1. **Mood Symptoms**

   - Persistent sadness, hopelessness, or a feeling of emptiness

   [redacted]

   [redacted]

2. **Anhedonia**

   - Marked loss of interest or pleasure in most daily activities

   [redacted]

   [redacted]

3. **Cognitive Symptoms**

   - Impaired concentration and indecisiveness

   [redacted]

   [redacted]

   [redacted]

4. **Neurovegetative Symptoms**

   - Sleep disturbances: insomnia (early or middle) or hypersomnia

   [redacted]

[redacted]

5. **Psychomotor Changes**

[redacted]

- Psychomotor agitation (restlessness, inability to sit still)

6. **Somatic Symptoms**

- Headaches, gastrointestinal disturbances, or nonspecific body aches

[redacted]

[redacted]

B. DSM-5 Diagnostic Criteria for Major Depressive Episode

[redacted]

[redacted]

[redacted]

- At least one of the symptoms must be either depressed mood or loss of interest/pleasure.

Table 3 Several standardized tools are used to assess and monitor depression

Tool	Purpose
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Treatment Modalities for Major Depressive Disorder (MDD)

The management of Major Depressive Disorder (MDD) requires a comprehensive, multidimensional, and patient-centered approach. [redacted]

The treatment strategies for MDD can be broadly categorized into:

- **Pharmacological therapies**: [redacted]

- **Psychotherapeutic approaches**:
- **Neuromodulation techniques**:
- **Supportive measures**:

Pharmacotherapy

Pharmacological therapy remains the cornerstone of management in moderate to severe MDD.

a. Selective Serotonin Reuptake Inhibitors (SSRIs)

- **Mechanism:**
- **Common agents:**
- **Side effects:**

b. Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

[redacted]

- **Common agents:** [redacted]
- **Side effects:** [redacted]

c. Tricyclic Antidepressants (TCAs)

TCAs are older agents that are effective but associated with significant **anticholinergic side effects** and **cardiotoxicity in overdose**.

- **Common agents:** [redacted]
- **Mechanism:** [redacted]
- **Side effects:** [redacted]

d. Monoamine Oxidase Inhibitors (MAOIs)

[redacted]

- **Examples:** [redacted]

e. Atypical Antidepressants

These include agents with unique mechanisms that are useful in specific clinical contexts:

- **Bupropion** (
- **Mirtazapine** (

f. Augmentation Strategies

- **Lithium**:
- **Atypical antipsychotics**:
- **Thyroid hormone (T3)**:
- **Stimulants or modafinil**: .

remission.

Psychotherapy

Psychological therapies are vital components of MDD management, particularly for mild to moderate depression, and as adjuncts in more severe cases.

a. Cognitive Behavioural Therapy (CBT)

CBT is the most studied and widely practiced psychotherapeutic modality for depression.

- **Core principle:** [redacted]
- **Techniques:** [redacted]
- **Duration:** [redacted].
- **Efficacy:** [redacted]

b. Interpersonal Therapy (IPT)

[redacted]

c. Behavioural Activation Therapy

[redacted]

d. Psychodynamic Therapy

[redacted]

[redacted]

[redacted]

[redacted]

e. Mindfulness-Based Cognitive Therapy (MBCT)

Combines mindfulness meditation with cognitive therapy principles.

[redacted]

[redacted]

[redacted]

Neuromodulation Therapies (ECT, rTMS, etc.)

[redacted]

[redacted]These therapies are often considered when patients have failed to respond to multiple adequate trials of pharmacotherapy and psychotherapy.

a. Electroconvulsive Therapy (ECT)

[redacted]

[redacted]

b. Repetitive Transcranial Magnetic Stimulation (rTMS)

[redacted]

- **Mechanism:** [redacted]
- **Indications:** [redacted]
- **Procedure:** [redacted]
- **Advantages:** [redacted]
- **Limitations:** [redacted]

c. Vagus Nerve Stimulation (VNS)

[redacted]

- **Mechanism:** [redacted]
- **Indications:** [redacted]

- **Limitations**

d. Deep Brain Stimulation (DBS)

- **Mechanism:**
- **Status:**
- **Limitations:**

e. Transcranial Direct Current Stimulation (tDCS)

- **Mechanism:**
- **Applications:**
- **Advantages:**
- **Limitations:**

f. Ketamine and Esketamine

Electroconvulsive Therapy (ECT)

Electroconvulsive Therapy (ECT) is a well-established and highly effective neuromodulation treatment for severe forms of Major Depressive Disorder (MDD), particularly when pharmacological and psychotherapeutic interventions have failed. [redacted]

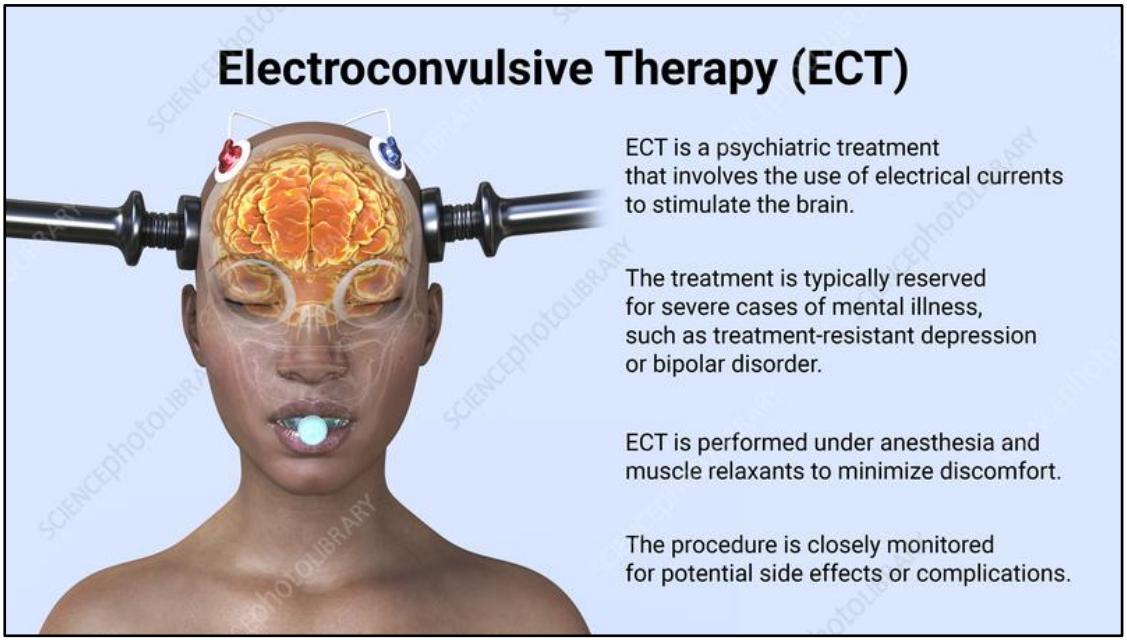


Fig 4 ECT (33)

[redacted]

Mechanism of Action

[redacted]

Neurotransmitter Regulation:

[redacted]

Neuroplasticity Enhancement:

[redacted]

Modulation of Functional Brain Networks:

[redacted]

Endocrine and HPA Axis Effects:

[redacted]

Anticonvulsant Effects:

[redacted]

Indications, Dosage, and Protocol

Indications for ECT in Depression:

- Severe or psychotic depression

Pre-treatment Evaluation:

- Thorough psychiatric and medical assessment

ECT Procedure Protocol:

Frequency:

Type: Modified ECT (

- **Electrode Placement:**

Bitemporal:

- **Unilateral (right-sided):** [redacted]

- **Stimulation Parameters:**

  [redacted]

Monitoring:

[redacted]

Side Effects and Limitations

[redacted]

Common Side Effects:

[redacted]

- **Cognitive effects:**

  - **Anterograde amnesia:** [redacted]

  - **Retrograde amnesia:** [redacted]

Long-term Cognitive Risks:

[redacted]

Medical Risks:

[redacted]

Advantages of ECT:

- Most rapid antidepressant effect of all available treatments

[redacted]

Limitations:

- Requires anaesthesia and hospital infrastructure

[redacted]

When used judiciously and under expert supervision, ECT provides rapid symptom relief and significant improvement in quality of life (32).

Ketamine in Depression

Ketamine, traditionally used as a dissociative anaesthetic, has recently emerged as a rapid-acting antidepressant, particularly effective in treatment-resistant depression (TRD).

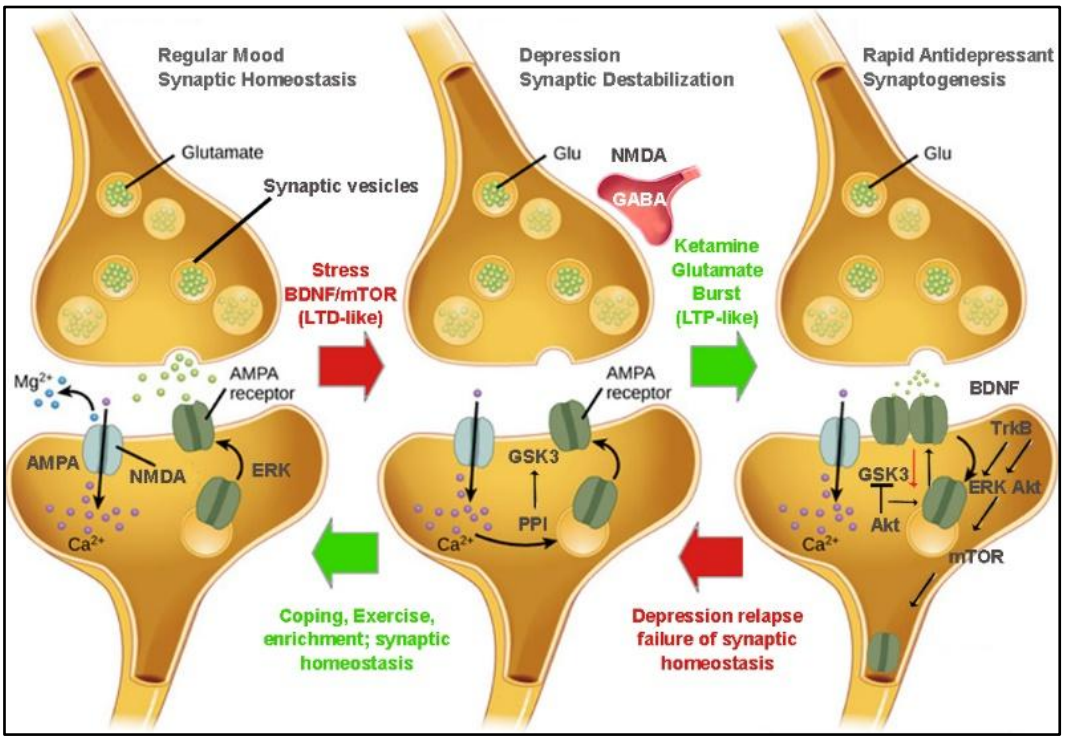


Fig 5 IV Ketamine (36)

[redacted]

Mechanism of Action

[redacted]

A. NMDA Receptor Blockade

[redacted]

B. Activation of mTOR Pathway

[redacted]

C. BDNF Elevation

[redacted]

D. Anti-Inflammatory and Neuroprotective Effects

[redacted]

E. Opioid Receptor Involvement

[redacted]

Routes of Administration (IV, Oral, IM, Nasal)

[redacted]

A. Intravenous (IV) Ketamine

- Standard and most studied form: 0.5 mg/kg infused over 40 minutes

[redacted]

B. Oral Ketamine

- Less bioavailability (20–30%), but useful in maintenance treatment or where IV access is difficult

[redacted]

C. Intramuscular (IM) Ketamine

- Useful in resource-limited settings

[redacted]

D. Intranasal Esketamine

- FDA-approved (2019) for TRD in conjunction with an oral antidepressant

[redacted]

1.9.3 Dosage, Efficacy, and Side Effects

A. Dosage

[redacted]**IV:** [redacted]

[redacted]**Oral:** [redacted]

[redacted]**Intranasal Esketamine:** [redacted]

B. Efficacy

- Rapid antidepressant effect observed in 60–70% of TRD patients

[redacted]

C. Side Effects(38)

Table 4 Adverse Effects of Ketamine in Depression Treatment

Common	Serious (Rare)
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

- No evidence of tolerance or withdrawal symptoms with short-term use in clinical settings

Limitations and Considerations

- Not first-line: Reserved for patients who fail standard treatments

[redacted]

[redacted]

While more long-term data are needed on maintenance, relapse prevention, and safety, current evidence positions ketamine as a promising alternative to ECT in selected patient populations (7).

Rationale for the Study

Major Depressive Disorder (MDD) is a debilitating mental illness that significantly impacts an individual's quality of life, functioning, and overall well-being. [redacted]

This has led to the classification of a significant subset of patients as having Treatment-Resistant Depression (TRD), a clinical condition associated with higher morbidity, risk of suicide, and increased healthcare costs (12).

Research Studies

[redacted] (2000) was the first controlled trial to demonstrate the rapid antidepressant effects of ketamine in patients with Major Depressive

Disorder (MDD). [redacted]

[redacted] (2012) explored the rapid antidepressant effect of ketamine in patients undergoing Electroconvulsive Therapy (ECT). [redacted]

[redacted] (2015) conducted a systematic review and meta-analysis to evaluate the efficacy and tolerability of ketamine as an adjunct to Electroconvulsive Therapy (ECT). [redacted]

[redacted]. (2015) performed a systematic review and meta-analysis evaluating the impact of etomidate, an alternative anaesthetic agent, on seizure duration in Electroconvulsive Therapy (ECT). [redacted]

[redacted]. (2016) systematically evaluated the adverse effects of Electroconvulsive Therapy (ECT), providing critical insights into the risk-benefit profile of this long-standing treatment for severe and treatment-resistant depression. [redacted]

[redacted]. (2019) conducted a randomized controlled trial comparing the efficacy of intravenous ketamine versus Electroconvulsive Therapy (ECT) in patients diagnosed with Major Depressive Disorder (MDD). [redacted]

[redacted]

[redacted]. (2019) conducted a randomized controlled trial comparing the efficacy of ketamine-assisted versus thiopentone-assisted ECT in patients with Major Depressive Disorder (MDD). [redacted]

[redacted]. (2020) carried out a prospective comparative study evaluating the antidepressant and cognitive effects of serial ketamine infusions versus ECT in patients with severe depression. [redacted]

[redacted]. (2020) investigated the rapid antidepressant and ant suicidal effects of three modalities: intramuscular ketamine, oral ketamine, and Electroconvulsive Therapy (ECT) in patients with

Major Depressive Disorder (MDD). [redacted]

[redacted] (2020) conducted a pilot randomized trial comparing the antidepressant efficacy of ketamine and ECT in patients with treatment-resistant depression (TRD). [redacted]

[redacted] (2021) conducted a systematic review to evaluate whether ketamine could serve as an alternative to ECT in patients with treatment-resistant depression. [redacted]

[redacted]

[redacted] (2022) conducted a randomized controlled trial to evaluate whether low-dose ketamine could improve the speed of recovery from depression in patients undergoing Electroconvulsive Therapy (ECT). [redacted]

[redacted] (2022) published a systematic review and meta-analysis in *JAMA Psychiatry* to compare the efficacy and safety of ketamine versus ECT in adults with Major Depressive Episode (MDE). [redacted]

[redacted] (2023) assessed head-to-head trials comparing ketamine and ECT in patients with Major Depressive Disorder (MDD). [redacted]

[redacted] (2023) conducted the KADS study, a randomized, double-blind, active-controlled trial comparing the efficacy and safety of repeated subcutaneous ketamine injections for treatment-resistant depression (TRD). [redacted]

[redacted] (2024) conducted a prospective comparative study on the effectiveness of ECT versus ketamine in treatment-resistant depressive disorder. [redacted]

[redacted]

[redacted] (2024) published a secondary analysis of a large randomized clinical trial comparing ketamine and ECT in patients with treatment-resistant depression (TRD). [redacted]

[redacted] (2025) conducted a meta-analysis of randomized controlled trials comparing intravenous ketamine and ECT for both Major Depressive Disorder (MDD) and bipolar depression. [redacted]

[redacted]The study advocated for ketamine as a frontline emergency

intervention and ECT as a long-term solution, particularly in chronic and severe cases (51).

MATERIAL AND METHODS

MATERIAL AND METHODS

SITE: [redacted]

PROPOSED DURATION OF STUDY:

[redacted]

SAMPLE: [redacted]

SAMPLE SELECTION: [redacted]

INCLUSION CRITERIA:

- [redacted]
- [redacted]

EXCLUSION CRITERIA:

- [redacted]
- [redacted]

[redacted]

MATERIAL: -

[redacted] **MADRS (Montgomery asberg depression rating scale):** [redacted]

- **MMSI (Modified scale for suicidal ideation):** [redacted]

[redacted] **HAM-**D (**Hamilton depression rating scale):** [redacted]

[redacted]

METHOD:

[redacted]

[redacted]

Organisation of Work Elements:

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

STATISTICAL CONSIDERATION:

[redacted]

[redacted]

[redacted]

RESULTS

RESULTS

Table 1: Comparison of Sociodemographic Between ECT and Ketamine Groups

Parameters		ECT (n=25)	Ketamine (n=25)	t/ χ2 Value p Value
Age (Mean ± SD)		[redacted]	[redacted]	[redacted]
Gender	Male	[redacted]	[redacted]	[redacted]
	Female	[redacted]	[redacted]	
Religion	Hindu	[redacted]	[redacted]	[redacted]
	Non-Hindu	[redacted]	[redacted]	
Marital Status	Married	[redacted]	[redacted]	[redacted]
	Single	[redacted]	[redacted]	
Type of family	Joint	[redacted]	[redacted]	[redacted]
	Nuclear	[redacted]	[redacted]	
Occupation	Employed	[redacted]	[redacted]	[redacted]
	Unemployed	[redacted]	[redacted]	

[redacted]

[redacted]

[redacted]

Table 2: Comparison of Clinical Indications for Intervention Between ECT and Ketamine Groups

Parameters		ECT (n=25)	Ketamine (n=25)	χ2 value, p value
Sessions				
Indication	Suicidal ideations	[redacted]	[redacted]	[redacted]
	Treatment resistant	[redacted]	[redacted]	

[redacted]

Table 3: Comparison of Duration of Illness Between ECT and Ketamine Groups

	ECT	Ketamine	F-value, p value
Duration of illness (in yrs.)	[redacted]	[redacted]	[redacted]

[redacted]

Table 4: Comparison of MADRS Scores Over Time Between ECT and Ketamine Groups

Group	Baseline	End of 1 week	End of 2 week	End of 3 week	End of treatment	F-value, p value
ECT (N: 23)	**30.83** ±6.11	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N :24)	**31.45** ±4.76	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
F value, p value	[redacted]					

[redacted]

[redacted]

[redacted]

Table 5: Comparison of MSSI Scores Over Time Between ECT and Ketamine Groups

Group	Baseline	End of 1 week	End of 2 week	End of 3 week	End of treatment	F-value, p value
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N :24)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
F value, p value	[redacted]					

[redacted]

[redacted]

[redacted]This indicates a substantial reduction in clinical severity as perceived by the clinician over the 4-week treatment course.

[redacted]

[redacted]

Table 6: Comparison of HAM-D Over Time Between ECT and Ketamine Groups

Group	Baseline	End of 1 week	End of 2 weeks	End of 3 weeks	End of treatment	F-value, p value
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N :24)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
F value, p value	[redacted]					

[redacted]

Table 7: Pre- and Post-Treatment Comparison of MADRS Scores and Percentage Improvement in ECT and Ketamine Groups in Treatment resistant depression

	MADRS Baseline	MADRS End of treatment	t value, p value	% of improvement
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N :24)	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Table 8: Pre- and Post-Treatment Comparison of MSSI Scores and Percentage Improvement in ECT and Ketamine Groups in treatment resistant depression.

	MSSI Baseline	MSSI End of treatment	T value, p value	% of improvement
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N :24)	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Table 9: Pre- and Post-Treatment Comparison of HAM-D Scores and Percentage Improvement in ECT and Ketamine Groups in treatment resistant depression.

	HAM D Baseline	HAMD End of treatment	t value, p value	% of improvement
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N :24)	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

Table 10: Pre- and Post-Treatment MADRS Scores and Percentage Improvement in ECT and Ketamine Groups in suicidal ideation.

	MADRS Baseline	MADRS End of treatment	t value, p value	% of improvement
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N :24)	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Table 11: Pre- and Post-Treatment Comparison of MSSI Scores and Percentage Improvement in ECT and Ketamine Groups in suicidal ideation

	MSSI Baseline	MSSI END	t value, p value	% of improvement
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N:24)	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Table 12: Pre- and Post-Treatment Comparison of HAM-D Scores and Percentage Improvement in ECT and Ketamine Groups in suicidal ideation

	HAM D baseline	HAM D end of treatment	t value, p value	% of improvement
ECT (N: 23)	[redacted]	[redacted]	[redacted]	[redacted]
Ketamine (N:24)	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

DISCUSSION

DISCUSSION

In the present study, the ECT and Ketamine groups were well matched in terms of age, gender, duration of illness, marital status, religion, occupation, and family type. [redacted]

[redacted]

[redacted](2024) (50) [redacted] (2020) (45)**,** which demonstrated that demographic variables did not confound clinical outcomes between ECT and Ketamine groups.

In both groups, the primary indication for intervention was treatment-resistant depression (TRD), with [redacted] patients (ECT) and [redacted] patients (Ketamine). [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

This pattern aligns with findings from [redacted] (37), where both ECT and Ketamine showed progressive reduction in MADRS scores, but ECT had a numerically greater decline over 4 weeks. Menon et al. [redacted]

[redacted]

[redacted](2024) (37), which failed to show clear superiority for either modality within short follow-up periods.

In the ECT group, MSSI scores decreased significantly from [redacted] to [redacted] while the Ketamine group showed a smaller but still significant reduction from [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

At the end of treatment, the patient with suicidal ideation the ECT group showed a statistically significant reduction in MADRS scores from [redacted]

These results are strongly supported by Sharma et al. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]Similarly, [redacted] (34) reported that while ketamine induced a faster initial reduction, the depth and durability of anti-suicidal effects were consistently greater with ECT**.**

Furthermore, de A. [redacted](2024) (37) also highlighted that Ketamine's effect on suicidal ideation is often transient, whereas ECT offers longer-lasting suppression, as demonstrated here.

[redacted]

[redacted] (47) concluded that while ketamine shows a faster onset of antidepressant action**,** ECT leads to deeper and more sustained symptom remission, particularly as measured by clinician-rated scales like HAM-D.

[redacted]

[redacted]

Thus, this subset analysis further supports the higher therapeutic gain with ECT, even when re-evaluating symptom reduction from a different baseline.

In this alternate analysis of [redacted] Both reductions were statistically significant, but the effect was more pronounced in the ECT group.

[redacted]

[redacted]

Thus, our findings support ECT as the more effective intervention for sustained relief from suicidal ideation in TRD patients.

In this comparison with treatment resistant depression, the ECT group showed a [redacted] reduction in HAM-D scores [redacted] Both groups improved significantly, but ECT again demonstrated superior efficacy.

[redacted]

[redacted] (2019) (43).

SUMMARY AND CONCLUSIONS

SUMMARY AND CONCLUSIONS

- This study aimed to evaluate and compare the clinical efficacy of ketamine and electroconvulsive therapy (ECT) in patients diagnosed with treatment-resistant major depressive disorder (TRD), including those presenting with active suicidal ideation.

[redacted]

[redacted]

- Future research involving larger sample sizes, longer-term follow-up, and stratification by illness severity may help refine treatment algorithms and identify subgroups that benefit most from each modality.

STRENGTHS AND LIMITATIONS

STRENGTHS AND LIMITATIONS

Strengths of the Study

- Well-matched baseline characteristics between ECT and Ketamine groups.

[redacted]

- Use of percentage improvement for direct effect size estimation.

Limitations

- Sample size was modest (n = 47 after attrition), limiting power for subgroup analyses.

[redacted]

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Proudman D, Greenberg P, Nellesen D. The Growing Burden of Major Depressive Disorders (MDD): Implications for Researchers and Policy Makers. Pharmacoeconomics. 2021 Jun 1

2. Reddy MS. Depression: The Disorder and the Burden. Indian J Psychol Med. 2010 Jan

[redacted]

[redacted]

[redacted]

51. Shi ZM, Lan XJ, Chen Q, Chen JJ, Su ZA, Huang XB, et al. Intravenous ketamine versus electroconvulsive therapy for major depressive disorder or bipolar depression: A meta-analysis of randomized controlled trials. J Affect Disord [Internet]. 2025 Feb 15

ANNEXURES

CASE RECORD PROFORMA

STUDY TITLE: "

Psychiatry Registration Number:

History:

[redacted]

[redacted]

केस रेकॉर्ड प्रोफॉर्म

अध्ययन शीर्षक: "[redacted]

मनोचिकित्सा पंजीकरण संख्या: _____

[redacted]

इतिहास:

[redacted]

मुख्य शिकायतें:

[redacted]

[redacted]

[redacted]

[redacted]

केस रेकॉर्ड प्रोफॉर्म

[redacted]

मानसोपचार नोंदणी क्रमांक: _____

[redacted]

इतिहास:

[redacted]

मुख्य तक्रारी:

[redacted]

[redacted]

[redacted]

PATIENT INFORMATION SHEET

Name of the topic:

[redacted]

[redacted]

[redacted]

PG Guide: Dr. **PG Student**: Dr.

रोगी सूचना पत्रक

[redacted]

रुग्ण माहिती पत्रक

[redacted]

INFORMED CONSENT FORM

STUDY TITLE:

[redacted]

Subject Name: _____ and/or **Age**:

_____

Date of birth: _____ (DD-MM-YY)

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Signature (or thumb impression) of the subject:

_____

Date: Day - Month – Year

Signatory's name: _____

Signature of the legally acceptable representative:

_____

Date: Day - Month - Year

Signatory's name: _____

Signature of an impartial witness: _____

Date: Day - Month - Year

Name of the impartial witness: _____

Signature of the Investigator: _____

Study Investigator's name: _____

Name of the Institution / Location: _____

Date: Day - Month - Year

सूचित सहमति पत्र

अध्ययन शीर्षक:

[redacted]

रोगी का नाम: _____ और/या **आयु**: _____

जन्म तिथि: _____ (दिन-माह-वर्ष)

[redacted]

रोगी के हस्ताक्षर / अंगूठे का निशान: _____

तारीख: दिन - माह - वर्ष

हस्ताक्षरी का नाम: _____

कानूनी रूप से स्वीकृत प्रतिनिधि के हस्ताक्षर: _____

तारीख: दिन - माह - वर्ष

नाम: _____

तटस्थ गवाह के हस्ताक्षर: _____

तारीख: दिन - माह - वर्ष

गवाह का नाम: _____

अन्वेषक के हस्ताक्षर: _____

अन्वेषक का नाम: _____

संस्थान / स्थान का नाम: _____

तारीख: दिन - माह – वर्ष

माहितीपूर्ण संमती फॉर्म

अभ्यासाचे शीर्षक:

[redacted]

रुग्णाचे नाव: _____ आणि/किंवा **वय**: _____

जन्म तारीख: _____ (दि-मा-व)

[redacted]

रुग्णाची सही / अंगठा ठसा: _____

तारीख: दिवस - महिना - वर्ष

सहिंदाराचे नाव: _____

कायदेशीर मान्य प्रतिनिधीची सही: _____

तारीख: दिवस - महिना - वर्ष

नाव: _____

तटस्थ साक्षीदाराची सही: _____

तारीख: दिवस - महिना - वर्ष

साक्षीदाराचे नाव: _____

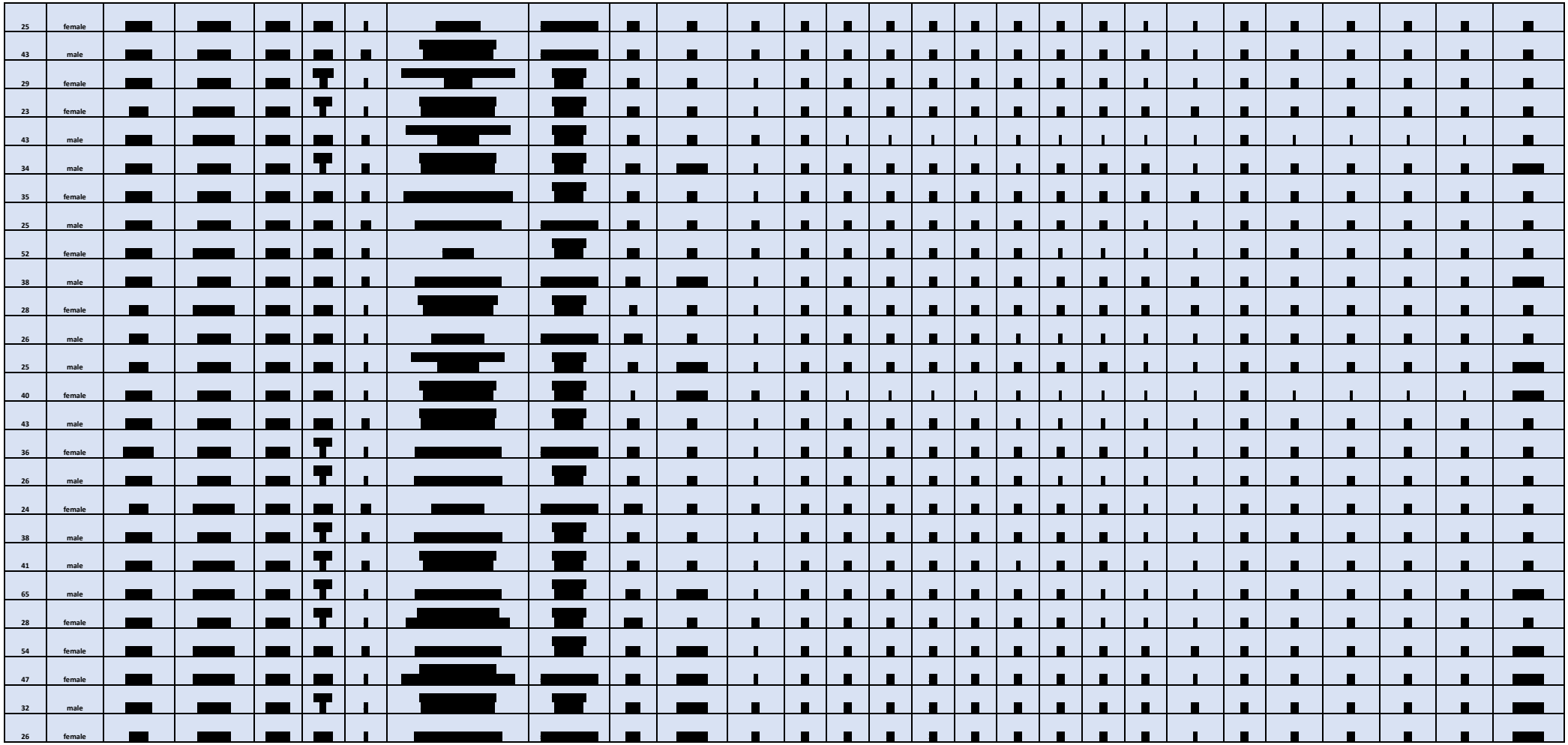
संशोधकाची सही: _____

संशोधकाचे नाव: _____

संस्था/स्थानाचे नाव: _____

तारीख: दिवस - महिना - वर्ष

AGE	GENDER	MARITAL STTAUS	OCCUPATION	FAMILY	RELIGION	DURATION OF	MEDICATION	INDICATION	dose	ketamine/ect	Session	MADRAS BL	MADRAS 1 WK	MADRAS 2WK	MADRAS 3WK	MADRAS EN	MSSI BL	MSSI 1WK	MSSI 2WK	MSSI 3WK	MSSI EN	HAM-DBL	HAM-D1 WK	HAM-D 2WK	HAM-D 3WK	HAM-D EN	ketamine/ect
28	male																										
55	male																										
22	female																										
25	female																										
65	male																										
29	female																										
30	female																										
26	female																										
42	female																										
60	male																										
18	female																										
49	female																										
50	female																										
63	female																										
45	female																										
45	male																										
37	female																										
19	male																										
38	male																										
33	female																										
25	female																										
58	male																										
24	female																										
33	male																										


25 female
43 male
29 female
23 female
43 male
34 male
35 female
25 male
52 female
38 male
28 female
26 male
25 male
40 female
43 male
36 female
26 male
24 female
38 male
41 male
65 male
28 female
54 female
47 female
32 male
26 female

The Modified Scale for Suicidal Ideation

[redacted]

[redacted]

Name_____ Total Score_____

Date_____

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

CUT-OFF INSTRUCTIONS - If Item 1 and Item 2 are scored less than "2" and Items 3 and 4 are scored 0, then STOP. Otherwise continue with full scale.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

1. Total Score = sum of the following items:

Item Number	Item Content	Score (0-3)
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
	[redacted]	
MSSI TOTAL SCORE:		_____

[redacted]

[redacted]

[redacted]

[redacted]

2. Criteria for "Serious Suicidal Ideation" - Must meet all of the following criteria

Characteristic	MSSI Criteria	Meets Criteria?
A. Severe suicidal ideation	MSSI Total Score > 20	Yes/No
B. Intense suicidal thoughts	Item 7 (Intensity) > 1	Yes/No
C. Actively Suicidal	Item 3 (Desire to make active attempt) > 1	Yes/No
D. Serious Plan	Item 15 (Method - Specificity) > 1	Yes/No

Meets Criteria for "Serious Suicidal Ideation?" (Must meet Criteria A-D above) **Yes/No**

Reference: **Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56–62**

Rating Clinician-rated

Administration time 20–30 minutes

Main purpose To assess severity of, and change in, depressive symptoms

Population Adults

Commentary

The HDRS (also known as the Ham-D) is the most widely used clinician-administered depression assessment scale. The original version contains 17 items ($HDRS_{17}$) pertaining to symptoms of depression experienced over the past week. Although the scale was designed for completion after an unstructured clinical interview, there are now semi-structured interview guides available. The HDRS was originally developed for hospital inpatients, thus the emphasis on melancholic and physical symptoms of depression. A later 21-item version ($HDRS_{21}$) included 4 items intended to subtype the depression, but which are sometimes, incorrectly, used to rate severity. A limitation of the HDRS is that atypical symptoms of depression (e.g., hypersomnia, hyperphagia) are not assessed (see SIGH-SAD, page 55).

Scoring

Method for scoring varies by version. For the $HDRS_{17}$, a score of 0–7 is generally accepted to be within the normal range (or in clinical remission), while a score of 20 or higher (indicating at least moderate severity) is usually required for entry into a clinical trial.

Versions

The scale has been translated into a number of languages including French, German, Italian, Thai, and Turkish. As well, there is an Interactive Voice Response version (IVR), a Seasonal Affective Disorder version (SIGH-SAD, see page 55), and a Structured Interview Version (HDS-SIV). Numerous versions with varying lengths include the HDRS17, HDRS21, HDRS29, HDRS8, HDRS6, HDRS24, and HDRS7 (see page 30).

Additional references

Hamilton M. Development of a rating scale for primary depressive illness. Br J Soc Clin Psychol 1967; 6(4):278–96.

Williams JB. A structured interview guide for the Hamilton Depression Rating Scale. Arch Gen Psychiatry 1988; 45(8):742–7.

Address for correspondence

Hamilton Depression Rating Scale (HDRS)

PLEASE COMPLETE THE SCALE BASED ON A STRUCTURED INTERVIEW

Instructions: for each item select the one "cue" which best characterizes the patient. Be sure to record the answers in the appropriate spaces (positions 0 through 4).

DEPRESSED MOOD *(sadness, hopeless, helpless, worthless)*

0 [_] [_] Absent

1 [_] [_] These feeling states indicated only on questioning.

2 [_] [_] These feeling states spontaneously reported verbally

3 [_] [_] Communicates feeling states non-verbally, i.e. through facial expression, posture, voice and tendency to weep.

4 [_] [_] Patient reports virtually only these feeling states in his/her spontaneous verbal and non-verbal communication.

2. FEELINGS OF GUILT

0 [_] [_] Absent

1 [_] [_] Self reproach, feels he/she has let people down.

2 [_] [_] Ideas of guilt or rumination over past errors or sinful deeds.

3 [_] [_] Present illness is a punishment. Delusions of guilt.

4 [_] [_] Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations.

3. SUICIDE

0 |__| Absent
1 |__| Feels life is not worth living.
2 |__| Wishes he/she were dead or any thoughts of possible death to self.
3 |__| Ideas or gestures of suicide.
4 |__| Attempts at suicide (any serious attempt rate 4).

4. INSOMNIA: EARLY IN THE NIGHT

0 |__| No difficulty falling asleep.
1 |__| Complains of occasional difficulty falling asleep, i.e. more than ½ hour.
2 |__| Complains of nightly difficulty falling asleep.

5. INSOMNIA: MIDDLE OF THE NIGHT

0 |__| No difficulty.
1 |__| Patient complains of being restless and disturbed during the night.
2 |__| Waking during the night – any getting out of bed rates 2 (except for purposes of voiding).

6. INSOMNIA: EARLY HOURS OF THE MORNING

0 |__| No difficulty.
1 |__| Waking in early hours of the morning but goes back to sleep.
2 |__| Unable to fall asleep again if he/she gets out of bed.

7. WORK AND ACTIVITIES

0 |__| No difficulty.
1 |__| Thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies.
2 |__| Loss of interest in activity, hobbies or work – either directly reported by the patient or indirect in listlessness, indecision and vacillation (feels he/she has to push self to work or activities).
3 |__| Decrease in actual time spent in activities or decrease in productivity. Rate 3 if the patient does not spend at least three hours a day in activities (job or hobbies) excluding routine chores.
4 |__| Stopped working because of present illness. Rate 4 if patient engages in no activities except routine chores, or if patient fails to perform routine chores unassisted.

8. **RETARDATION** (slowness of thought and speech, impaired ability to concentrate, decreased motor activity)

0 |__| Normal speech and thought.
1 |__| Slight retardation during the interview.
2 |__| Obvious retardation during the interview.
3 |__| Interview difficult.
4 |__| Complete stupor.

9. AGITATION

0 |__| None.
1 |__| Fidgetiness.
2 |__| Playing with hands, hair, etc.
3 |__| Moving about, can't sit still.
4 |__| Hand wringing, nail biting, hair-pulling, biting of lips.

10. ANXIETY PSYCHIC

0 |__| No difficulty.
1 |__| Subjective tension and irritability.
2 |__| Worrying about minor matters.
3 |__| Apprehensive attitude apparent in face or speech.
4 |__| Fears expressed without questioning.

11. ANXIETY SOMATIC (physiological concomitants of anxiety) such as:

gastro-intestinal – dry mouth, wind, indigestion, diarrhea, cramps, belching
cardio-vascular – palpitations, headaches
respiratory – hyperventilation, sighing
urinary frequency
sweating
0 |__| Absent.
1 |__| Mild.
2 |__| Moderate.
3 |__| Severe.
4 |__| Incapacitating.

12. SOMATIC SYMPTOMS GASTRO-INTESTINAL

0 |__| None.
1 |__| Loss of appetite but eating without staff encouragement. Heavy feelings in abdomen.
2 |__| Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for gastro-intestinal symptoms.

13. GENERAL SOMATIC SYMPTOMS

0 |__| None.
1 |__| Heaviness in limbs, back or head. Backaches, headaches, muscle aches. Loss of energy and fatigability.
2 |__| Any clear-cut symptom rates 2.

14. GENITAL SYMPTOMS (symptoms such as loss of libido, menstrual disturbances)

0 |__| Absent
1 |__| Mild
2 |__| Severe

15. HYPOCHONDRIASIS

0 |__| Not present
1 |__| Self-absorption (bodily)
2 |__| Preoccupation with health
3 |__| Frequent complaints, requests for help, etc.
4 |__| Hypochondriacal delusions.

16. LOSS OF WEIGHT *(RATE EITHER a OR b)*

a) According to the patient:

0 |__| No weight loss.
1 |__| Probable weight loss associated with present illness.
2 |__| Definite (according to patient) weight loss.
3 |__| Not assessed.

b) According to weekly measurements:

0 |__| Less than 1 lb weight loss in week.
1 |__| Greater than 1 lb weight loss loss in week.
2 |__| Greater than 2 lb weight loss in week.
3 |__| Not assessed.

17. INSIGHT

0 |__| Acknowledges being depressed and ill.
1 |__| Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
2 |__| Denies being ill at all.

Total score: |__|__|

Montgomery and Asberg Depression Rating Scale (MADRS)

[redacted]

---

1. Apparent Sadness

[redacted]

---

2. Reported sadness

[redacted]

3. Inner tension

[redacted]

4. Reduced sleep

[redacted]

5. Reduced appetite

[redacted]

6. Concentration Difficulties

[redacted]

7. Lassitude

[redacted]

8. Inability to feel

[redacted]

9. Pessimistic thoughts

[redacted]

10. Suicidal thoughts

[redacted]