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Review Paper

Current Advances in The Diagnosis and Treatment of Mood Disorders

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ABSTRACT

Mood disorders, which include Major Depressive Disorder (MDD) and Bipolar Disorder (BD), rank among the top three global disability causes while creating substantial public health challenges. A considerable number of patients fail to achieve treatment results because they do not respond to established pharmacological and psychotherapeutic treatments. The review investigates present-day diagnostic and treatment methods for mood disorders through examination of neurobiology and diagnostic methods and new treatment developments which began emerging during the last ten years. Research indicates that genetic risks together with neuroplasticity and inflammatory pathways and microbiota-gut-brain connections build the foundation of how diseases develop. The field of diagnostics has made advancements through the development of DSM-5-TR and ICD-11 criteria updates which combined with biomarker and multi-omics methods and digital phenotyping and artificial intelligence tools enhance assessment accuracy and early diagnosis capabilities. The treatment field has entered a new phase which includes rapid-acting antidepressants that contain esketamine and neurosteroids and psychedelic-assisted therapy and next-generation cognitive behavioral therapy and neuromodulation methods that use transcranial magnetic stimulation and deep brain stimulation. The research specifically examines perinatal and geriatric populations while it maintains focus on accessibility problems and cost issues and ethical dilemmas that persist in the field. The psychiatric field is evolving toward precision psychiatry which uses personalized data-based approaches to improve results and decrease worldwide disease impact while providing fresh possibilities to patients who experience treatment-resistant mood disorders

INTRODUCTION

Mood disorders represent psychiatric disorders which produce major interruptions to a person's emotional state and lead to episodes of depression

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and episodes of mania. The Global Burden of Disease Study 2019 identified depressive and anxiety disorders as accounting for the highest proportion of the global mental health burden with depression alone affecting approximately 3.8% of the world's population [1]. Medical professionals have used patient symptom descriptions together with their medical assessments to make diagnoses which follow established protocols found in the DSM and ICD manuals throughout history. The biological differences that exist between these disorders make it difficult to accurately diagnose patients who have unipolar or bipolar depression which results in poor treatment results. The "trial-and-error" method used in pharmacotherapy leads to remission for only one-third of patients following their first-line antidepressant test [2]. This review investigates the current transformation of psychiatric medicine which shifts from using descriptive diagnoses toward implementing mechanistic treatment methods. Our research demonstrates progress in identifying genetic and inflammatory causes of diseases and shows how diagnostic standards have been improved in the DSM-5-TR and ICD-11 and we showcase the groundbreaking development of fast-acting treatment methods and customized brain stimulation techniques.

2. Pathophysiology and Etiology

2.1 Genetic Factors

Mood disorders demonstrate a strong heritable component which research has established. The Psychiatric Genomics Consortium conducted recent large-scale Genome-Wide Association Studies which discovered more than 178 genetic risk loci for MDD while they advanced our comprehension of Bipolar Disorder genetic structure [3]. The research demonstrates that mood disorders follow a polygenic inheritance pattern because they involve numerous common genetic variants which all have minimal impact on the condition.

2.2 Neurobiological Mechanisms

Current scientific understanding considers traditional monoaminergic theories (which include serotonin and norepinephrine and dopamine) as inadequate. Researchers have redirected their attention toward studying the glutamate system together with its effects on neuroplasticity. The neurotrophic hypothesis of depression identifies Brain-Derived Neurotrophic Factor (BDNF) deficiencies together with hippocampal and prefrontal cortex atrophy as its main elements. The Microbiota-Gut-Brain Axis (MGBA) functions as a key mood regulator while gut dysbiosis affects neurodevelopment and stress responses [4].

2.3 Inflammatory and Immune Pathways

A subset of mood disorders has been identified as an inflammatory disorder which requires further research. Elevated pro-inflammatory cytokines (e.g., IL-6, TNF-alpha) can cross the blood-brain barrier, altering neurotransmitter metabolism and inducing "sickness behavior" that mimics depression [5]. The condition of immunometabolic dysregulation shows highest occurrence in treatment-resistant depression (TRD) combined with metabolic syndromes.

3. Advances in Diagnostic Approaches

3.1 Clinical Diagnostic Criteria Updates

The DSM-5-TR Text Revision and ICD-11 release have established more precise diagnostic boundaries. The ICD-11 systematizes mood disorders by merging all disorders under one main category and establishing simplified diagnostic standards which can be used worldwide. The system defines "mixed" symptoms together with "anxious distress" which functions as a specifier

instead of a separate diagnosis [6]. The DSM-5-TR introduced "Prolonged Grief Disorder" while it explained "Unspecified Mood Disorder" to assist doctors in identifying cases that fall below standard diagnostic thresholds [7].

3.2 Biomarkers and Multi-Omics

There is no single diagnostic biomarker for this condition, but multi-omic panels have shown potential for diagnostic testing. The combination of proteomic and metabolomic profiling enables researchers to discover biological markers that define inflammatory depression, which helps determine the effectiveness of anti-inflammatory treatments used as supplementary interventions [5]. The field of pharmacogenomic testing has become more common for predicting drug metabolism through CYP450 enzyme analysis, despite ongoing debates about its validity, because it helps to minimize adverse reactions and determine optimal medication dosages [8].

3.3 Digital Phenotyping and Wearable Tech

Digital phenotyping enables researchers to conduct real-time studies of human progress by using data collected from personal electronic devices. Researchers can use smartphone data which includes GPS tracking and typing speed and voice acoustic measurements to achieve precise predictions of depressive and manic episode relapses [9]. The system enables ongoing observation which supports the implementation of adaptive interventions that occur at the exact moment they are needed.

3.4 Machine Learning (ML) & AI

Machine learning algorithms are being trained to differentiate Bipolar Disorder from MDD, a common clinical pitfall. A recent meta-analysis showed that ML models which combined neuroimaging data with clinical data could identify these medical conditions at a sensitivity rate of 0.84, which exceeded the performance of standard clinical methods [10].

4. Advances in Treatment

4.1 Pharmacologic Treatments

4.1.1 Rapid-Acting Antidepressants

Eskatinine, which is the S-enantiomer of ketamine, became the most important pharmacological advancement of the last three decades. The substance functions as an NMDA receptor antagonist because it is delivered through intranasal administration which induces fast synaptic growth through the mTOR pathway [11]. The FDA now approves the medication for Treatment-Resistant Depression (TRD) and major depressive disorder (MDD) with acute suicidal thoughts which provides patients with relief that begins within hours instead of needing weeks to develop.

4.1.2 Neurosteroids

The FDA approved Zuranolone in 2023 as a rapid-acting oral neuroactive steroid which functions as a GABA-A receptor positive allosteric modulator specifically for Postpartum Depression (PPD) treatment. Zuranolone functions as a short 14-day treatment which delivers prolonged remission to patients in need of urgent perinatal care, which separates it from standard antidepressant treatments [12].

4.1.3 Psychedelics

Psilocybin-assisted therapy is about to receive its first clinical approval. The 2022 trial established that a 25mg psilocybin dose together with psychological support helped TRD patients decrease their depression scores more effectively than control subjects, although participants

experienced adverse events which included nausea and temporary headache [13].

4.2 Psychotherapeutic Interventions

Cognitive Behavioral Therapy (CBT) remains the gold standard. A 2023 meta-analysis confirmed CBT's efficacy is comparable to pharmacotherapy for moderate depression but superior in preventing relapse [14]. "Third-wave" therapies, including Acceptance and Commitment Therapy (ACT) and Mindfulness-Based Cognitive Therapy (MBCT), are increasingly validated for preventing recurrence. The implementation of Next-Generation CBT (NG-CBT) through AI-powered chat-bots and application-based training modules has proven successful in delivering mental health services to underserved populations who lack sufficient resources [15].

4.3 Neuromodulation Techniques

4.3.1 SAINT Protocol (TMS

The Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) has changed the way Transcranial Magnetic Stimulation (TMS) operates. SAINT uses high-dose intermittent theta-burst stimulation for 5 days while standard protocols require a 6-week period to deliver treatments. Open-label trials show that almost 80% of patients with severe TRD reach remission according to study results [16].

4.3.2 Deep Brain Stimulation (DBS)

DBS requires surgeons to place electrodes inside designated brain areas such as subcallosal cingulate and ventral capsule with ventral striatum. The latest clinical trials use tractography to create personalized targeting systems that map white matter pathways. Long-term follow-up studies prove that DBS treatment delivers long-lasting results for patients who have exhausted every alternative therapy including ECT [17].

5. Special Populations

5.1 Perinatal and Postpartum

Postpartum depression (PPD) affects up to 17% of mothers. Screening guidelines have become more stringent than they existed before Zuranolone. The untreated state of PPD creates serious repercussions for infant development which makes it essential to identify and treat the condition without delay [12].

5.2 Geriatric Mood Disorders

Elderly depression presents itself through physical symptoms and cognitive dysfunction which resembles "pseudodementia". Vascular depression which shows white matter hyperintensities needs doctors to treat both cardiovascular risk factors and antidepressant medications with strong intensity [1].

6. Challenges and Limitations

The study needs extra research because existing results show that people with disability face ongoing challenges. The expense of new treatments which include Esketamine and SAINT TMS together with their requirement for specialized medical facilities creates access problems that affect lower-income patients [11 16]. The use of biomarkers shows potential but no biomarker has become a standard diagnostic tool for medical practice. The medical field continues to use syndromic diagnosis methods [7]. Digital phenotyping creates major ethical issues which involve both patient monitoring and the question of who holds data rights [9].

7. FUTURE DIRECTIONS

The future of mood disorder management depends on Precision Psychiatry. The system will enable doctors to determine suitable treatments for patients through its use of genomic risk scores and inflammatory markers together with digital phenotype information (the system will help doctors choose between anti-inflammatory drugs for patients with elevated CRP levels and cognitive behavioral therapy for patients who have particular cognitive distortions). The gut microbiome research shows that "psychobiotics" (probiotics which provide mental health advantages) will soon become supplementary treatments [4]. The destigmatization of psychedelic medicine may create new methods for helping persistent patients achieve brain plasticity [13].

CONCLUSION

The landscape of mood disorders is undergoing rapid changes at this time. The medical field has progressed from discovering medications by chance to developing medications through specific scientific methods. The approval of rapid-acting agents like esketamine and zuranolone together with the SAINT protocol and digital diagnostics enables a completely new treatment approach. The existing implementation gaps hinder progress because these tools offer unique chances to reduce suffering for millions who experience mood disorders.

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