

Major Depressive Disorder: a General Overview

Tianqi Wang

SILC Business School, Shanghai University, Shanghai, 200000. China

Abstract. Major Depressive Disorder (MDD) has become a serious mental health problem with a lifetime prevalence of 15% to 20%. MDD is associated with significant morbidity, mortality, disability, and negative influence on patient's daily life. This article is an overview of MDD, including its etiology, impacts, treatments, and recommendations for future perspective. The paper's results and discussion section will list the possible causes of MDD from biological, physiological, and social perspectives, such as physical active level and sleeping quality. Along with its impacts on individuals in social relationship, health and financial status. The article will also list several common treatment methods, for example, antidepressants, Electroconvulsive Therapy, and cognitive-behavioral therapy. Then provide some details regarding the perspective for the future. Overall, the readers could have a general overview to MDD. This paper is a review based on researches and studies collected using Google Scholar and PubMed Central in the field of MDD. Fundamental information about MDD is obtained from the Diagnostic and Statistical Manual of Mental Disorders: 5th edition. For the etiology section, the primary source is Dean's study, which provides comprehensive information about the etiology of MDD. The overview of treatment is based on Li's study, which provides a clinical guideline on MDD treatment process. The article will also reference several other academic sources such as Cui's study and Mullen's study in order to provide a comprehensive overview of MDD.

1 Introduction

MDD, also called major depression and clinical depression. According to DSM-5, this mood disorder is typified by an all-encompassing and enduring bad mood, along with low self-esteem and a diminished interest or enjoyment in often pleasurable activities [1]. About 16.6% of people are afflicted by MDD over their lifetime [2]. The average age of beginning for depression in woman is 32 years old, and they are 70% more likely than men to develop it during their lifetime. A person needs to have at least five of the symptoms listed above for at least two weeks in order to be diagnosed with MDD. Either a low mood or an inability to find enjoyment in once-enjoyed activities must be one of the symptoms. The symptoms must materially disrupt one or more aspects of the person's life, for example, work and school, and must not be directly caused by medical condition or the use of substances. The symptoms are link to persistent sad, anxious, feelings of hopelessness or pessimism, worthlessness, helplessness, or self-hatred. Furthermore, according to Mullen. MDD is increasingly recognized in children and adolescents [3]. MDD frequently first manifests in adolescence and has a strong correlation with suicidality [2]. Epidemiological studies suggest that the lifetime prevalence of MDD in adolescents can reach up to 20% by the end of adolescence, with a lower prevalence in childhood. The

research also shows a noticeable increase around puberty, which suggests that hormonal changes, among other factors, might play a role in the development of depression.

In summary, the primary focus of this paper is to provides and overall review on the etiology, impacts, treatments, and future perspective of depressive disorder.

2 Results and discussion

2.1 Etiology

One of the most prevalent mental illness in recent years is MDD. However, it is important to note that MDD, and its onset is often due to the interaction of several different factors rather than a single cause [4]. According to DSM-5, three categories could be used to classify the causes of depression: Precipitating causes, perpetuating causes, and predisposing causes [1].

2.1.1 Precipitating causes

The precipitating causes describes an immediate triggers that initiate an individual's depressive episodes. These triggers are varied and can be categorized into three main types: acute physical stresses, psychological stresses, and social stresses. Acute physical stresses include diseases or infections that could have a profound

Corresponding author: Tianqi.Wang-1@student.uts.edu.au

impact on an individual's mental health. Chronic conditions including diabetes, cancer, and cardiovascular disease, for example, have been related to a higher chance of getting depression. The research between 3559 AYA cancer patients and 35590 matched controls shows the result that adolescent and young adult patients with cancer had a three-fold higher risk for MDD [5]. The physical discomfort, limitations on daily activities, and the emotional toll of dealing with a serious health condition can serve as significant stressors. For psychological stresses, the loss of loved one can lead to profound sadness and grief, which could evolve into depression for some individuals. This type of stress could challenge an individual's coping mechanisms and potentially trigger a depressive episode. Furthermore, social stresses include work problems, significant changes in social status, or alterations in living conditions. For example, losing a job for undergoing a divorce could have a significant impact on an individual's psychological well-being. The estimated frequency of MDD among US adults has risen from 7.1% to 7.8%, according to study, as a result of the higher unemployment rate during the Covid-19 pandemic [6]. Events of this nature might give rise to depressive symptoms such as hopelessness, isolation, and worthlessness.

2.1.2 Perpetuating causes

Perpetuating causes of MDD are factors that not only worsen the current condition of an individual but also have the potential to push someone deeper into the throes of depression. Physical inactivity is a known perpetuating factor for depression. Lack of exercise could lead to decrease in endorphin levels, which are natural mood lifters, and could exacerbate feelings of low self-esteem and hopelessness. Regular physical activity, on the other hand, has been shown to have a protective effect against the development of depression and could be an effective part of a treatment plan. Furthermore, Co-occurring emotional disorders, such as anxiety or personality disorders, could also perpetuate depressive symptoms. These disorders could intensify the symptoms of depression, making more challenging to treat, and often require a comprehensive treatment approach that addresses all co-occurring conditions. Moreover, continuous exposure to psychological or social stresses, such as chronic work stress, ongoing relationship problems, or long-term financial difficulties, could perpetuate depression. These stresses could create a persistent state of emotional turmoil, leading to a deepening of depressive symptoms over time. In addition, sleep disturbances, including insomnia or hypersomnia, are common in individuals with depression and could serve as both a precipitating and perpetuating factor. Poor sleep could exacerbate depressive symptoms, leading to a vicious cycle where depression leads to sleep problems, which in turn make the depression worse.

2.1.3 Predisposing causes

Predisposing causes of MDD include a variety of genetic and environmental factors that increase an individual's risk of developing the condition. These factors interact in complex ways, often setting the state for the disorder's onset in the presence of precipitating and perpetuating factors. Research has consistently shown that genetics play a crucial role in the risk of developing depression [4]. A hereditary component might be present in those who have a family history of depression since they are more susceptible. The recent family, twin, and adoption studies also indicates that the genetic factors has a crucial effect in the occurrence of MDD [7]. This genetic predisposition indicates that certain individuals are more vulnerable to depression due to their genetic makeup, which affects neurotransmitter systems involved in mood regulation. Also, environmental factors, including one's upbringing and exposure to stressors, also significantly contribute to the predisposition to depression. Growing up in a lower socioeconomic status could expose individuals to chronic stress, limited access to mental health resources, and increased exposure to environmental stressors—all of which could increase the risk of developing depression. Furthermore, gender could be a risk factor, as women are statistically more likely to develop depression than men. This difference is thought to result from a combination of hormonal, social, and psychological factors that uniquely affect women. Additionally, if the etiology of a depressive disorder could be linked to the direct physiological effects of a psychoactive drug or other chemical substance, the disorder might be considered substance-induced.

2.2 Related factors

According to Zheng's research, in traditional research, personal and sociodemographic factors are considered to be related to the MDD [8]. For example, physical activities, smoking, level of education, sleeping quality, and body mass index.

2.2.1 Physical activities

Physical activities could be a factor which is linked to MDD. The unhealthy behaviour, such as predominantly sedentary behavior, has increased continuously across age groups, especially in the majority of the young population [9]. A primarily sedentary lifestyle with 4-8 hours of sitting per day has been linked to poor mental and physical health outcomes, according to research based on studies for a variety of health indicators, such as metabolic and mental/psychological indicators. According to further research in 14091 teenagers, excessive sitting lifestyle raises the chance of developing long-term mental and physical illness like MDD [10]. According to a recent representative poll of individuals in Germany, adults spend roughly eight hours a day sitting down, which is strongly suggested to be a risk

factor for mental health [11]. Herbert indicates that the university students could be considered as an emerging adults group with long daily sitting time, which brings the risk of mental disorders. The international studies has approved that the university students' daily sitting time are 6.4 to 11.25 hours in average, which might lead to the rising rates of mental health issues and stress perception among college students globally [8].

2.2.2 Sleeping quality

Sleep is another putative MDD pathway. Insomnia could be as candidate mediator in explaining the progress of MDD across extended timeframes, due to its negative effect on economic and physical condition, such as becoming overly dependent on medical care and missing work [12].

Previous studies have looked into the theory that lower sleep quality is a predictor of depression symptoms [13]. For example, a one-year follow-up research based on the Pittsburgh Sleep Quality Index (PSQI) and the Depression Anxiety Stress Scale-21 (DASS-21), has demonstrated that, among 686 Chinese male college students, poor sleep quality predicted a higher incidence of depression symptoms [14]. Similarly, studies on young adult women conducted over a nine-year period show that sleep problems played a role in the development, maintenance, and recurrence of depression disorders. [15]. Relatedly, based on the self-rated questionnaire PSQI, among Swiss individuals, a potential association was found between poor sleep quality and subsequent depression episodes over a 20-year period [16]. The assumption of the link between insomnia and MDD could be considered as plausible based on these results of research.

2.3 Impact

The impact of MDD is profound and multifaceted, affecting individuals' psychological, physical, social, and economic well-being [17].

Psychological impact is one potential effect. MDD is associated with significant psychological distress, including persistent sadness, hopelessness, and a lack of interest in previously enjoyed activities. It can lead to diminished self-esteem and self-worth, increased risk of suicide, and a substantial decline in life satisfaction. Also, MDD is linked to various physical health problems, including chronic pain, sleep disturbances, changes in appetite and weight, and increased risk of cardiovascular diseases. The disorder can worsen the outcomes of existing chronic conditions like diabetes and hypertension.

Furthermore, MDD might cause social and relationship impact. Individuals with MDD often experience difficulties in maintaining relationships, withdrawing from social interactions, and facing challenges in their familial and romantic relationships. The disorder can lead to social isolation, affecting the

individual's support system and exacerbating the condition.

The economic impact of MDD includes increased healthcare utilization, reduced productivity, and higher rates of unemployment. It is one of the main causes of disability in the globe and accounts for a large portion of the financial and disease burden. Additionally, the MDD will significantly influence the patients ability on emotion control, which will negatively decrease work efficiency. Similar problems on emotion regulation might link to unemployment which damage patients' financial status.

Moreover, MDD may have an impact on cognitive abilities. Cognitive faculties including memory, concentration, and decision-making could be hampered by MDD. These cognitive deficits can affect the individual's daily functioning, work performance, and quality of life.

Overall, the quality of life of individuals with MDD is significantly affected. The disorder impacts their ability to function effectively in work, school, and social environments, leading to a diminished overall quality of life.

2.4 Treatment

For treatment, electroconvulsive therapy, medicine, and psychotherapy are the three most popular therapies for depression.

Cognitive-behavioral therapy (CBT) is now the most effective type of psychotherapy for depression. CBT enables patients to modify counterproductive behaviors and confront persistent, self-defeating thought patterns. Trained professionals such as psychologists, psychiatrists, social workers, licensed therapists, and family therapists could effectively deliver these therapies in a number of settings (inpatient or outpatient, group-based or individual) [2].

The alternative is medication; practically all of the prior antidepressants were unintentionally found a few decades ago due to current insufficient understanding of the etiology and pathophysiology of depression [18]. While antidepressants are generally considered safe and effective, they come with several challenges, such as the onset of their effects often taking up to two weeks and potential side effects that can hinder adherence to the treatment regimen. Furthermore, less than half of patients with depression achieve full remission even after undergoing optimized treatments that may include a combination of multiple medications and psychotherapy. Over recent years, the quest for new antidepressants has primarily targeted the enhancement of serotonin or norepinephrine receptor specificity, aiming to achieve quicker, safer, and more effective outcomes. Consequently, there was a pressing demand for innovative strategies to develop antidepressants that not only act faster and are safer but also have greater efficacy.

Furthermore, neuromodulation therapy could be an option. Neuromodulation therapy utilizes technologies such as magnetic pulses, micro-currents, or neural

feedback mechanisms within specific treatment parameters to target the central or peripheral nervous system. This approach aims to modulate the balance between excitatory and inhibitory neuronal activities, thereby alleviating or diminishing the symptoms associated with certain conditions [18]. Electroconvulsive Therapy (ECT) ranks as one of the most effective treatments for severe depression, enhanced by the use of safer equipment and improved methods, such as modified ECT procedures. Evidence from randomized controlled trials (RCTs) and meta-analyses has also demonstrated the safety and efficacy of repetitive Transcranial Magnetic Stimulation (rTMS) in treating depression. Additionally, newer approaches like transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), vagal nerve stimulation, deep brain stimulation, and light therapy have shown promise in treating depression. However, some of these treatments remain largely in the experimental phase and have not yet been broadly adopted in clinical practice.

Additionally, physical activity could be an option as a treatment of MDD. According to study, physical activity counselling could improve lifestyle physical activity and cardiorespiratory fitness in people with MDD, who are frequently thought to suffer from both mental and physical health issues [19]. In Blumenthal's research, in a trial involving 202 adult MDD patients, he examined if a 4-month aerobic exercise regimen was more beneficial than antidepressant medication [20]. As compared to a placebo control condition, the results show that both medication and exercise reduce depressive symptoms in a comparable way and have higher rates of remission. Overall, there is no certain therapy has a decisive therapeutic effect to MDD. The CBT is the most used clinical approach, but its effect is depends on personal adaptability of patients. The antidepressant has rapid onset as its advantage, but it has side-effect and has to be continuously used to achieve optimal therapeutic effect, which brings the problem of addiction. The neuromodulation is a potential cure to MDD since it has become the most effective therapy to serve depression. However, as a innovative technology which target on nervous system and brain, the further research and clinical trails is necessary.

3 Conclusion

In conclusion, MDD could be contributed to biological, psychological, and social factors, but more researches are needed to be done to find out which of them could be the key factor. Unfortunately, MDD had hazardous impacts on the patients, including negative effect on physical, physiological, social, and economical field. Appropriate treatment, for example, psychotherapy, medication, and neuromodulation therapy, are necessary for patient to avoid negative consequences.

Over the last decade, there has been significant advancement in the understanding of depression. Yet, the complexity of the disorder, variability in how individuals respond to treatments, and the challenges in

bridging research findings to clinical practice remain substantial obstacles. The central issue lies in the incomplete understanding of the causes and underlying mechanisms of depression, limiting the ability to deepen the knowledge of the disorder and, consequently, develop more effective treatments. The diversity within the condition itself—manifesting in different symptoms and responses to treatment across patients—complicates the development of universally effective treatments. Additionally, while there have been improvements in therapeutic strategies, finding effective treatments for all patients is still a challenge. The gap in translational medicine, which involves applying discoveries from basic research to clinical applications, further complicates the ability to efficiently introduce new and effective treatment modalities. These issues underscore the need for continued research and innovation in the field of depression.

References

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Arlington : American Psychiatric Association
2. D.R. Neavin, J. Joyce, C. Swintak, **6**(2), 48 (2018)
3. S. Mullen, *Ment Health Clin*, **8**(6), 275-283 (2018)
4. J. Dean, M. Keshavan., *Asian J Psychiatr*. **27**,101-111 (2017)
5. T. Akechi, I. Mishiro, S. Fujimoto. *Psychooncology*. **31**(6), 929-937 (2022)
6. P. Greenberg, A. Chitnis, D. Louie, E. Suthoff , SY. Chen , J. Maitland, P. Gagnon-Sanschagrin, AA. Fournier, RC. Kessler. *Adv Ther*. **40**(10), 4460-4479 (2023)
7. L. Cui , S. Li, S. Wang, X. Wu, Y. Liu, W. Yu, Y. Wang, Y. Tang, M. Xia, B. Li. *Signal Transduct Tar.*, **9**(1), 30 (2024)
8. X. Zheng, L. Tong, C. Zhang, C. Zhang ,C. Zhang,B. Wan., *PLoS One*, **18**(8), e0289419 (2023)
9. C. Herbert. *Front Public Health.*, **25**, 10. (2022)
10. A. Kandola, G. Lewis, D.P.J. Osborn, B. Stubbs, JF. Hayes, *Lancet Psychiat.*, **7**, 262–71 (2020)
11. I. Froböse, B. Biallas, B. Wallmann-Sperlich. *Der DKV-Report 2018 Wie gesund lebt Deutschland*. (2018), Available online at: <https://fis.dshs-koeln.de/en/publications/der-dkv-report-2018-wie-gesund-lebt-deutschland>
12. A.G. Harvey, G. Murray, R.A. Chandler& A. Soehner, *Clin Psychol Rev*, **31**(2), 225–235 (2011)
13. V.V. Nguyen, N.H. Zainal, M.G. Newman, *J Anxiety Disord*. **90**, 102601. (2022)
14. P. Zou, X. Wang, L. Sun, K. Liu, G. Hou, W. Yang, & Q. Chen. *J Psychosom Res*, 136, Article 110177 (2020)
15. M.L. Jackson, E.M. Sztendur, N.T. Diamond, J.E. Byles& D. Bruck, *Archives of Women' s Mental Health*, **17**(3), 189 – 198 (2014)

16. D.J. Buysse, J. Angst, A. Gamma, V. Ajdacic , D. Eich& W. Rössler, *Sleep*, **31**(4), 473 - 480 (2008)
17. World Health Organization. Depression and other common mental disorders: global health estimates. Geneva: World Health Organization.
18. Z. Li, M. Ruan, J. Chen,Y. Fang, *Neurosci Bull.* **37**(6), 863-880 (2021)
19. M. Gerber, J. Beck, S. Brand, R. Cody, L. Donath, A. Eckert, O. Faude, X. Fischer, M. Hatzinger, E. Holsboer-Trachsler, C. Imboden, U. Lang, S. Mans, T. Mikoteit, A. Oswald, U. Pühse, S. Rey, A.K. Schreiner, N. Schweinfurth, U. Spitzer, L. Zahner., *Trials.* 20(1), 367 (2019)
20. J.A. Blumenthal, M.A. Babyak, P.M. Doraiswamy, L. Watkins, B.M. Hoffman, K.A. Barbour, S. Herman, W.E. Craighead, A.L. Brosse, R. Waugh, A. Hinderliter, A. Sherwood. *Med.* **69**(7), 587-96 (2007)