

## Depression Review: Factors and Perspectives

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### Abstract

Depression is largely experienced in our societies. It is costly and highly prevalent medical condition having a lifetime prevalence of around 16% in US adults. Around 13.5 million adults got major depressive disorder in the last year and 34 million will get it at some point. Women experience it more likely about 1.5 to 3 times greater than men. Anyone can experience it at any age but most people experiences first episode in their early thirties. This review represents different factors that are associated with depression.

**Keywords:** Depression, types, genetics, sleep, neurogenesis.

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### INTRODUCTION

Depression is a serious and common medical ailment affecting one's feelings, thinking and actions. It causes loss of interest in activities that once was enjoyable. It may lead to many physical and emotional problems and may decrease work and home functioning of a person resulting in reduced productivity [1]. It may influence relationships and chronic health conditions including asthma, diabetes, cancer, cardio-vascular disease and many others. Feeling low and sad at different times in our life is normal but if it becomes miserable and hopeless than it should be treated, if left untreated, it may lasts for years and may aggravate overtime [2]. Several medical conditions like some vitamin deficiency and thyroid problem may imitate symptoms of depression [1].

In a survey by Villanueva in 2013, relation between abnormal neurogenesis with major depressive disorder was studied and found that alterations of individual factors including hypothalamic-pituitary-axis, miRNAs expression, pro inflammatory cytokines production, growth factor and neutrophins production and even the delivery of abnormal GI signaling peptides can significantly induce mood alterations [3].

### DIAGNOSTIC CRITERIA FOR DEPRESSION

Depression is defined as having anhedonia or sad mood, which persists nearly throughout the day or every day for at least 14 days or two weeks. For diagnosis, an additional four symptoms are needed including weight loss or gain, loss of energy or fatigue, difficulty in decision-making, thoughts of

worthlessness, sleep disruptions, speeding up or slowing down of physical movements, recurrent thoughts of suicide or death. All individuals do not possess the same symptoms. The duration, severity and frequency can also differ among individuals and vacillate in the same individual over time [4].

### TYPES OF DEPRESSION:

There are many forms of depression. The DSM-V lists nine different types of depression [5].

#### Major Depression

Major depression is a frequent and complex psychiatric illness that airs frequent challenges to patient as well as physicians. It is a widespread disorder [5]. This type of depression is the most prevalent form. In this type, patient experiences recurrent events during their lives [6]. It is usually treated with antidepressants. Talk therapy is also beneficial [7].

#### Dysthymia

It is defined as persistent depressed mood for a long period [6]. Dysthymia responds better to talk therapy in contrast to medications. Their combination is also suggested by some studies [7].

#### Seasonal Affective Disorder

This type of depression produces due to deficiency of sunlight [6]. SAD is a frequent depressive disorder comprises of a seasonal pattern, with an onset in fall and continued to winter months. Symptoms centered on low energy and sad mood. Females are more prevalent; those that are younger, having family

history of depression, SAD or bipolar disorder and live distant from equator. Treatment typically includes antidepressants, Vitamin D, light therapy and counseling [8].

### Atypical Depression

Patient may experience irritability, relationship problems and heaviness feeling in their limbs [6]. Talk therapy works great in treating this type of depression as suggested by different studies [7].

### Bipolar Disorder

Bipolar is also known as manic-depressive illness; episodes of mania and depression strike the patient at different times [6]. Combining antidepressant drugs with psychosocial treatments can increase acute stabilization and long-term maintenance of depression. Medications affecting circadian rhythm and sleep have been found to affect mood and would be helpful in selecting treatment regimens for individual patients [9].

### Psychotic Depression

In psychotic depression, patient becomes catatonic due to the presence of hallucinations and delusions [6]. According to different reviews published earlier, combination of antidepressant and antipsychotic was more effective in this type of depression [7].

### Post-partum Depression

It affects approximately 10-15% of mothers annually. This type of depression often occurs from months to a year following birth [10]. However a study reported postpartum depression after 4 years from birth [11]. Causes of post-partum depression include situational, physiological or multifactorial factors [12].

Previous history of post-partum depression [13] and single parenthood [14] are some of the triggering factors. Combination of medications and talk therapy are usually prescribed [7].

### Premenstrual Dysphoric disorder

It is a severe mood disorder characterized by physical and cognitive-affective symptoms in one week before menses. It affects a large number of women worldwide [15-17]. Pharmacotherapy is recommended as a first line treatment as stated by the American College of Gynecology [18].

### Situational Depression

It is triggered by any event [6]. It is also called reactive depression. It originates from a feeling that results from a particular situation. If the symptoms last for more than six months, it may lead to long term depression. It is a treatable condition. Antidepressants, psychotherapy or their combination can be employed [19].

## RISK FACTORS FOR DEPRESSION

Anyone can be affected by depression, even an individual who's living relatively in an ideal condition. Different factors have a role in depression;

### Biochemistry

Variations in the levels of different chemicals in brain may promote symptoms of depression.

### Personality

People having low self-esteem or stressed people seem to be more liable to experience depression [1].

### Genetics of Depression

Depression is cognizant to run in families, declared that different factors genetically contribute to the risks of disease development. Uptil now, very little is known regarding genetic basis of depression. According to some studies, variations in some genes with a minor effect contribute to the risk of developing disease. These variations may be somewhat different between women and men. The genes thought to be consociated have diverse functioning in brain like synthesis, transportation and activities of neurotransmitters. Other genes associated with depression are engaged in the growth, maturation and the maintenance of neurons as well as synapses between neurons to adopt change over time, a feature described as synaptic plasticity [20]. Candidate gene includes *SLC6A3*, *5HTT/SLC6A4*, *APOE*, *MTHFR*, *DRDA*, *HTRIA* and *GNB3* [21].

### Environmental Factors

These factors play critical role in arising depression like certain medications, substance abuse, stressful life events for example death of a beloved, divorce, etc. There may be other factors like social isolation, relationship difficulties, financial problems, childhood neglect or abuse and many others. Some disease such as thyroid disease, cancer and chronic pain are also consociated with an enhanced risk of depression development [22]. It is likely that genetic factors interact with environmental factors to conclude the risk of developing depression [21].

## PREVALENCE OF DIABETES

The prevalence of diabetes has been increasing more rapidly in low and middle-income countries. Prevalence of people with diabetes has increased from 108 million (1980) to 422 million (2014). Worldwide, among adults, 18 years of age and above has increased from 4.7% (1980) to 8.5% (2014) [23-25].

## ROLE OF DIABETES IN DEPRESSION

It has been supposed that diet could play a major role in depression [26]. A variety of nutrients are required for the modulation and synthesis in the neurotransmission system and so they are involved in mood regulation [27, 28]. Each nutrient has its own

biochemistry and has a role in mood regulation that is discussed elsewhere [29].

Anglin R. E *et al.*, in 2013 declare an association of depression and vitamin-D. The findings are consistent with their hypothesis that decreased vitamin- D concentrations is consociated with depression [30].

### **CELLULAR & MOLECULAR BASIS OF DEPRESSION**

Many brain regions likely mediate the vast symptoms of depression. An autopsy reported of depressed patients found abnormalities in those brain regions, but due to some contradictory findings there is a need to investigate various mechanisms of mood regulation related to different brain areas. It has been found that the brain areas involved in depression are the same involved in addiction [31].

Stress has a major role in the initiation of psychiatric disease, like depression and anxiety. A study suggested p11 as a primal molecule in cell type specific stress-induced depression [32].

### **DEPRESSION & CIRCADIAN RHYTHM**

Major depression is often affiliated with alteration in circadian rhythm, secretion of hormones including melatonin, cortisol and core temperature [33]. Previous studies have found that disturbed circadian rhythm is associated with major depressive disorder. However, light can affect mood through non-circadian mechanisms and brain lesions disrupts cells and remove important neuronal connections, which includes light reception pathways [34].

Improper light may cause circadian rhythm alterations with sleep disruptions that finally may lead to depression like state and mood disorder [35].

### **DEPRESSION & INFLAMMATION**

Inflammatory illness is consociated with depression. Human studies have shown a relevant role of chemokines in depression. In earlier reviews chemokines were found altered in depressed people. Chemokines were found to have neurobiological effect and by leukocyte recruitment and trafficking, they have known to be consociated with depression [36].

Depression and schizophrenia are consociated with inflammatory processes. Previous studies show that these diseases display higher level of pro-inflammatory markers. In a study, serum levels of interleukin 18, interleukin 6, tumor necrosis factor and interleukin 2 were obtained in schizophrenic and depressed patients and compared with the control. It was found that the levels of all these markers are significantly increased and significantly stimulated which shows the inflammatory characteristic of these disorders [37].

Adaptive or innate immune system interacts with neurocircuits and neurotransmitters to impact the peril for depression [38].

### **EXERCISE & DEPRESSION**

Previous studies had shown that people having major depressive disorders are less active physically and approx. two third of them did not meet physical activity requirements [39]. In another study, comparison of exercise versus control group was observed. The findings declared that exercise had a significant and large impact on in depressive people. The study claimed exercise as evidence based anti depressant treatment [40]. Ranjbar *et al.*, in 2015 declare that both aerobic and anaerobic exercises are beneficial in reducing symptoms of depression and enhancing positive mood in depressive patients [41].

### **DEPRESSION & ACUPUNCTURE**

Smith C. A *et al.*, in March 2018 declare that acupuncture is very effective for depression as it may result in moderate decline in the severity of depression as compared to usual treatment or in untreated conditions. Risks of adverse effects are unclear when treating with acupuncture [42].

### **METHODOLOGY**

For this article, a computerized search of Pubmed, WHO and related articles from 2005 to 2018 was reviewed for determination of literature. A search strategy was developed using combination of word terms: depression, seasonal depression, major depressive disorder, circadian rhythms, sleep disorders, sleep disturbances, gene expressions, antidepressants, agomelatine and melatonin, exercise. Systematic reviews and control studies were examined to gather the data available for depression.

### **CONCLUDING REMARKS**

Depression is considered as a common disorder and is ranked third as a major cause of disability after cardiac and respiratory ailments [43]. It is the major cause of many disables conditions like blindness, heart attacks, stroke, and kidney failure. WHO declares diabetes as the seventh highlighted cause of death in 2016. Healthy and balanced diet, regular physical activity and avoiding use of tobacco are some important measures to prevent the onset of diabetes [44].

This review reflects the relation between abnormal neurogenesis with major depressive disorder and it was analyzed that alterations in individual factors like hypothalamic-pituitary-axis, miRNAs expression, pro inflammatory cytokines production, growth factor and neutrophins production and even the delivery of abnormal GI signaling peptides can significantly induce mood alterations that may lead towards depression [3].

In depression, sleep disturbance is the major symptom that affects daytime working of people. Sleep difficulties are often a key factor that drives a depressed patient to seek help medically [45]. In this review we have discussed that medicines affecting melatonin and sleeping behavior have a positive impact on depression. They are employed in treating depression and have less adverse effects as compared to conventional antidepressants.

Further research is required to effectively identify factors and strategies for prevention and treatment of depression.

#### DECLARATIONS

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#### Conflict of Interest

There is no conflict of interest associated with this work.

#### Contribution of Authors

The authors named in this article prepared this manuscript and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

#### REFERENCES

- Parekh, R. (2017). American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5), Fifth edition. 2013.
- Legg, T. J. (2016). Depression Overview, health-line newsletter.
- Villanueva, R. (2013). Neurobiology of major depressive disorder. *Neural plasticity*, 2013.
- Halverson, J., Beevers, C., & Kamhoiz, B. (2016). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5) Clinical Practice Review for Major Depressive Disorder*. Anxiety and Depression association of America.
- Culpepper, L., Muskin, P. R., & Stahl, S. M. (2015). Major depressive disorder: understanding the significance of residual symptoms and balancing efficacy with tolerability. *The American journal of medicine*, 128(9), S1-S15.
- Cagliostro, D. (2018). Depression; Persistent Sadness & Loss of Interest in Life.
- Illiades, C., & Keegan K. (2018). 9 Different Types of Depression, Everyday Health.
- Melrose, S. (2015). Seasonal Affective Disorder: An Overview of Assessment and Treatment Approaches; *Depress Res Treat*. 178564.
- Geddes, J. R., & Miklowitz, D. J. (2013). Treatment of bipolar disorder. *The lancet*, 381(9878), 1672-1682.
- Anokye, R., Acheampong, E., Budu-Ainooson, A., Obeng, E. I., & Akwasi, A. G. (2018). Prevalence of postpartum depression and interventions utilized for its management. *Annals of general psychiatry*, 17(1), 18.
- Mauthner, N. S. (1998). Re-assessing the importance and role of the marital relationship in postnatal depression: Methodological and theoretical implications. *Journal of Reproductive and Infant Psychology*, 16(2-3), 157-175.
- Fishel, A. H. (2004). Mental health disorders and substance abuse. *Maternity & women's health care*, 960-82.
- Leopold, K. A., & Zoschnick, L. B. (1997). Women's Primary Health Grand Rounds at the University of Michigan: Postpartum Depression. *Female Patient-Total Health Care For Women*, 22, 12-30.
- Andrews-Fike, C. (1999). A review of postpartum depression. *Primary care companion to the Journal of clinical psychiatry*, 1(1), 9.
- Dennerstein, L., Lehert, P., & Heinemann, K. (2012). Epidemiology of premenstrual symptoms and disorders. *Menopause international*, 18(2), 48-51.
- Epperson, C. N., Steiner, M., Hartlage, S. A., Eriksson, E., Schmidt, P. J., Jones, I., & Yonkers, K. A. (2012). Premenstrual dysphoric disorder: evidence for a new category for DSM-5. *American Journal of Psychiatry*, 169(5), 465-475.
- Hantsoo, L., & Epperson, C. N. (2015). Premenstrual dysphoric disorder: epidemiology and treatment. *Current psychiatry reports*, 17(11), 87.
- ACOG. (2001). Practice Bulletin Premenstrual syndrome. Clinical management guidelines for obstetrician-gynecologists. *International Journal Obstetric Gynecology*, 73:183-191.
- Palkhivala, A. (2017). Depression, situational depression, University health news.
- NIH. (2018). Depression, Genetics home reference, U.S. National Library of Medicine.
- Flint, J., & Kendler, K. S. (2014). The genetics of major depression. *Neuron*, 81(3), 484-503.
- Sparling, T. M., Henschke, N., Nesbitt, R. C., & Gabrysch, S. (2017). The role of diet and nutritional supplementation in perinatal depression: A systematic review. *Maternal & child nutrition*, 13(1).
- Emerging Risk Factors Collaboration. (2010). Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *The Lancet*, 375(9733), 2215-2222.
- Bourne, R. R., Stevens, G. A., White, R. A., Smith, J. L., Flaxman, S. R., Price, H., ... & Pesudovs, K. (2013). Causes of vision loss worldwide, 1990–

- 2010: a systematic analysis. *The lancet global health*, 1(6), e339-e349.
25. USRDS. (2014). Epidemiology of kidney disease in the United States. MD; 188-210.
  26. Kaplan, B. J., Crawford, S. G., Field, C. J., & Simpson, J. S. A. (2007). Vitamins, minerals, and mood. *Psychological bulletin*, 133(5), 747-760.
  27. Rechenberg, K., & Humphries, D. (2013). Nutritional interventions in depression and perinatal depression. *The Yale journal of biology and medicine*, 86(2), 127-137.
  28. Bodnar, L. M., & Wisner, K. L. (2005). Nutrition and depression: implications for improving mental health among childbearing-aged women. *Biological psychiatry*, 58(9), 679-685.
  29. Leung, B. M., & Kaplan, B. J. (2009). Perinatal depression: prevalence, risks, and the nutrition link—a review of the literature. *Journal of the American Dietetic Association*, 109(9), 1566-1575.
  30. Anglin, R. E., Samaan, Z., Walter, S. D., & McDonald, S. D. (2013). Vitamin D deficiency and depression in adults: systematic review and meta-analysis. *The British journal of psychiatry*, 202(2), 100-107.
  31. Icahn School of Medicine at Mount Sinai. (2018). Molecular Basis of Addiction and Depression.
  32. Seo, J. S., Wei, J., Qin, L., Kim, Y., Yan, Z., & Greengard, P. (2017). Cellular and molecular basis for stress-induced depression. *Molecular psychiatry*, 22(10), 1440-1447.
  33. Plesničar, B. K. (2014). Efficacy and tolerability of agomelatine in the treatment of depression. *Patient preference and adherence*, 8, 603-612.
  34. Landgraf, D., Long, J. E., Proulx, C. D., Barandas, R., Malinow, R., & Welsh, D. K. (2016). Genetic disruption of circadian rhythms in the suprachiasmatic nucleus causes helplessness, behavioral despair, and anxiety-like behavior in mice. *Biological psychiatry*, 80(11), 827-835.
  35. LeGates, T. A., Fernandez, D. C., & Hattar, S. (2014). Light as a central modulator of circadian rhythms, sleep and affect. *Nature Reviews Neuroscience*, 15(7), 443-454.
  36. Leighton, S. P., Nerurkar, L., Krishnadas, R., Johnman, C., Graham, G. J., & Cavanagh, J. (2018). Chemokines in depression in health and in inflammatory illness: a systematic review and meta-analysis. *Molecular psychiatry*, 23(1), 48.
  37. Al-Hakeim, H. K., Al-Rammahi, D. A., & Al-Dujaili, A. H. (2015). IL-6, IL-18, sIL-2R, and TNF $\alpha$  proinflammatory markers in depression and schizophrenia patients who are free of overt inflammation. *Journal of affective disorders*, 182, 106-114.
  38. Miller, A. H., & Raison, C. L. (2016). The role of inflammation in depression: from evolutionary imperative to modern treatment target. *Nature reviews immunology*, 16(1), 22-34.
  39. Schuch, F., Vancampfort, D., Firth, J., Rosenbaum, S., Ward, P., Reichert, T., ... & Stubbs, B. (2017). Physical activity and sedentary behavior in people with major depressive disorder: a systematic review and meta-analysis. *Journal of affective disorders*, 210, 139-150.
  40. Schuch, F. B., Vancampfort, D., Richards, J., Rosenbaum, S., Ward, P. B., & Stubbs, B. (2016). Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. *Journal of psychiatric research*, 77, 42-51.
  41. Ranjbar, E., Memari, A. H., Hafizi, S., Shayestehfar, M., Mirfazeli, F. S., & Eshghi, M. A. (2015). Depression and exercise: a clinical review and management guideline. *Asian journal of sports medicine*, 6(2), e24055.
  42. Smith, C. A., Armour, M., Lee, M. S., Wang, L. Q., & Hay, P. J. (2018). Acupuncture for depression. *Cochrane database of systematic reviews*, (3).
  43. Ibrahim, A. K., Kelly, S. J., Adams, C. E., & Glazebrook, C. (2013). A systematic review of studies of depression prevalence in university students. *Journal of psychiatric research*, 47(3), 391-400.
  44. WHO. (2018). Diabetes.
  45. Kasper, S., Hajak, G., Wulff, K., Hoogendijk, W. J., Luis Montejo, A., Smeraldi, E., ... & Baylé, F. J. (2010). Efficacy of the novel antidepressant agomelatine on the circadian rest-activity cycle and depressive and anxiety symptoms in patients with major depressive disorder: a randomized, double-blind comparison with sertraline. *Journal of Clinical Psychiatry*, 71(2), 109-120.