

Factors inducing depression as effective tool in therapy

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Abstract

Depression being a psychological disorder is known to cause morbidity and mortality of the concerned individual globally. According to an estimate from the World Health Organisation (WHO), about 57 million people equivalent to about 18% of the global population are suffering from depression in India. There are several known factors responsible for inducing depression in humans such as abusing drugs and alcohol, overwork, poor diet, using excess caffeine or sugar, lack of exercise, poor sleep, sexual abuse, genetic disorders, sadness, physical health issue, brain chemistry imbalance, lack of confidence, rejection/loneliness, loss of loved one etc. According to an epidemiological data, 30~40% of occurrences of depressive disorder involve genetic factors. Consequently, environmental factors also play significant role in development of depression. Studies have shown that cognitive therapy is as efficacious as antidepressant medications in treating depression which is believed to reduce the risk of relapse even after its discontinuation. Cognitive therapy and antidepressant medication probably engage some similar neural mechanisms, as well as mechanisms that are distinctive to each. Extensive research is therefore needed to delineate the population suffering from a specific kind of factor inducing depression which may help develop adequate therapy to treat the patients quickly and effectively.

Introduction

The level of stressors in the life of humans is ever on increase in modern era since very transition from childhood, puberty and adulthood making them susceptible to development of psychological disorders finally leading to depression [1]. The adolescents develop depression due to many factors including loss of a very close relative, unfavourable behaviour conducted by step mother or father, drug abuse and bullying or teasing etc. On the other hand, in adults the depression may crop up due to brain chemistry imbalance, genetic disorders, drugs and alcohol abuse, lack of exercise and confidence, loss of loved ones, loss of motivation overwork, poor diet, physical health issue, use of excess caffeine or sugar, poor sleep, sexual abuse, sadness, rejection/loneliness, etc.

In Japan, psychological disorders have been included among the four major diseases such as cancer, diabetes, heart disease and stroke [2]. According to an estimate from WHO, about 300 million people are currently suffering from depression globally which counts for 4.3% of the world's population. The available reports suggest that till 2020 about 4.3% of Indian population and 10~15% of Japanese population may suffer from depression [3].

Therefore, addressing depression represents an urgent challenge. This article provides a brief overview and recent advances on different aspects of depression and possible remedial measures to treat this psychosomatic disorder in humans.

Forms of depression

There are five common forms of depression such as (1) **Major depression**—having symptoms of depression most of the day, nearly every day for at least 2 weeks that interfere with your ability to work, sleep, study, eat, and enjoy life. An episode can occur only once in a person's lifetime, but more often, a person has several episodes. (2) **Persistent depressive disorder (dysthymia)**—having symptoms of depression that last for at least 2 years. A person diagnosed with this form of depression may have episodes of major depression along with

periods of less severe symptoms. Some forms of depression are slightly different, or they may develop under unique circumstances, such as. (3) **Perinatal Depression:** Women with perinatal depression experience full-blown major depression during pregnancy or after delivery (postpartum depression). (4) **Seasonal Affective Disorder (SAD):** SAD is a type of depression that comes and goes with the seasons, typically starting in the late fall and early winter and going away during the spring and summer. (5) **Psychotic Depression:** This type of depression occurs when a person has severe depression plus some form of psychosis, such as having disturbing false fixed beliefs (delusions) or hearing or seeing upsetting things that others cannot hear or see (hallucinations). Other examples of depressive disorders include disruptive mood dysregulation disorder (diagnosed in children and adolescents) and premenstrual dysphoric disorder. Depression can also be one phase of bipolar disorder (formerly called manic-depression). But a person with bipolar disorder also experiences extreme high—euphoric or irritable—moods called “mania” or a less severe form called “hypomania” [4].

Causes of depression: Major causes of occurrence of depression in people include the patients suffering from cancer, chronic pain, diabetes, or other such chronic diseases are increasingly likely to become depressed as disease severity increases [5-8]. Obsessive, melancholic, and other such personality types have also been associated with susceptibility to depression [9]. It may also be caused by drugs that are used in treatment of physical diseases. These therapeutic drugs are diverse and include anti-hypertensive drugs, hormone drugs, anti-ulcer drugs, anti-tuberculosis drugs, anti-Parkinson's disease drugs, immunomodulatory drugs, and psychotropic drugs [10].

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Genetic factors associated depression: When an immediate family (parents, children, or siblings) includes a person with depression, the familial incidence is 1.5 to 3 times higher [11,12]. Research with identical twins has also shown that when one twin develops depression, the probability that the other twin will also develop depression is 25 to 93% [13]. These reports imply that in some cases, genetic factors may play a role in the onset of depression. Studies examining postmortem brains of and, thus, they are not broken down by proteasomes. As a result, there is an overabundance of transporter, and more uptake of serotonin in the synaptic cleft. Accordingly, the amount of free serotonin is reduced. The aforementioned abnormal behaviors were attenuated by sertraline, a serotonin transporter inhibitor. Imipramine also mitigated some of the abnormal behaviours [14].

Currently, depression is diagnosed by a psychiatrist based on patient symptoms. However, approximately 80% of new patients seek consultation from a doctor of internal medicine but do not receive a proper diagnosis. If we could provide biomarkers for diagnosis of depression similar to blood glucose for that of diabetes, even a general physician could make a diagnosis. Because patients with intractable depression have diminished amounts of ubiquitinated serotonin transporter in their lymphocytes, we have applied for a patent and propose the possibility that the amount of ubiquitinated serotonin transporter may be a biomarker for depression diagnoses [15].

Lifestyle factors and environmental causes of major depression: Physical health is an important foundation of mental health. People who are not physically healthy are at an increased risk for developing depression. People who engage in unhealthy lifestyle practices also have a more difficult time overcoming depressive episodes than healthier people, as their unhealthy lifestyle practices tend to work against many treatment effects. Negative lifestyle factors that can contribute to a depressive episode or drag one out include: (1) **Abusing drugs and alcohol**-- The disease outcomes chosen for the current analysis were depression, panic disorder, post-traumatic stress disorder (PTSD), alcohol abuse/ dependence, drug abuse/dependence and suicide attempts. Evidence for causality came from twin studies, prospective studies and representative community studies. In particular, the three twin studies available provided strong evidence of a causal relationship as they inherently controlled for the genetic and family environment factors that are also associated with mental disorders [16-18]. These studies provide evidence of significant associations between panic disorder, alcohol abuse/dependence, drug abuse/dependence and suicide attempts and depression. (2) **Poor diet, including excess caffeine or sugar**- If a person is suffering from low mood, feels tense and irritable, is tired all the time, tends to comfort eat, has sleeping problems and a reduced interest in sex, and some of the above apply, the chances are they are short on serotonin. Depression as a biochemical phenomenon, best dealt with by antidepressant medication. However, there is a third aspect to the onset and treatment of depression that is given little heed: nutrition. One factor that often underlies depression is poor control of blood glucose levels. The symptoms of impaired blood sugar control are many, and include fatigue, irritability, dizziness, insomnia, excessive sweating (especially at night), poor concentration and forgetfulness, excessive thirst, depression and crying spells, digestive disturbances and blurred vision [19].

The most accepted biochemical theory explaining the root cause of aforesaid psychosomatic imbalances relies on perturbations in the metabolism of two types of neurotransmitters in brain: (1) the metabolism of serotonin which is a mood enhancer and it is synthesised using Tryptophan as a precursor amino acid, and (2) the metabolism of

adrenaline, dopamine and nor-adrenaline which influence motivation and are synthesised using phenylalanine as a precursor amino-acid. In cases of depression, these amino acids are given two to three times each in 100mg dose of 5-HTP every time to the affected individual. Sometimes, this regimen is supplemented with different vitamins such as B12 and folic acid and minerals, which are thought to be involved in synthesis of serotonin from 5-HTP.

Other factors causing depression in any individual may include (1) **Poor sleep**-Sleep disturbance is one of the key symptoms of this disease, which may even act as a key factor posing risk to suicide. Therefore a deep sleep for such patients is recommended as it may help recover from depression to certain extent [20]. (2) **Sexual abuse**- There are evidences which indicate a close relationship between depression and sexual abuse, which is characterised as inappropriate and undesirable sexual solicitation such genital touching or fondling; or penetration in terms of oral, anal or vaginal intercourse or attempted intercourse of a child by an aged perso [21]. (3) **Genetic depression and role of candidate genes**- As established by meta-analysis, about 20 genes have been found to be associated with onset of depression [22]. (4) **Health issues**- Depression have also been shown to be emerged and linked with the physical illness of an individual as tested by a study primarily in women [23-25]; though such an association between depression and physical illness may be highly nonspecific and unbiological [26]. (5) **Perturbations in brain chemistry**- The development of chemical imbalance in brain also contributes as a key player in depression. The perturbations in the metabolism of monoamines which act as neurotransmitters in central nervous system (CNS) may offer suitable explanations for emergence of depression. Any alterations in its complex metabolic pathway may result occurrence of subtle changes in synthesis, storage, release, and deactivation of monoamines [27]. Several workers have reported that most of the application of antidepressants helps recover such patients from mental illness by re-establishment of chemical balance in brain via enhancing the levels of monoamines [28,29]. (6) **Rejection and Loneliness**: Loneliness has been found to develop symptoms of depression as they lose happiness and become pessimistic [30,31]. In the patients suffering from depression due to loneliness gradually develop negative feelings and wrong judgement of personality (7). **Loss of loved one**: Another important cause of depression could be the unexpected loss of loved one which exerts plenty of stress on the person concerned and it may destabilise his/her mental balance and may result into psychiatric disorders [32,33]. A summary of these factors has been presented in Table 1.

Additional Factors

Environmental factors: Various environmental factors including physical or chemical have also been reported to immensely contribute in the onset of depression among the people. The anthropogenic or synthetic chemicals, such as food additives and preservatives, pesticides, hormones and drugs, and many industrial wastes become part of the environment and get mixed into air, water, soil, food item and animal/plant products. These chemical factors have been reported to cause depression after reaching into the food chain and getting accumulated into body systems. The physical environmental factors causing depression may include noise pollution, radiations, natural disasters such as destructive hurricanes, tsunamis, and earthquakes, and several other dangerous environmental events. Electrical pollution caused by radio waves produced by electrical equipments is invisible, silent, odourless, and tasteless but not fit for health. These factors may generate symptoms of depression including muscle twitches and cramps, and severe breathlessness (Figure 1).

Table 1. A summary of different factors involved in depression

Factors	Actions
Abusing drugs and alcohol	Panic disorder, post-traumatic stress disorder (PTSD)
Poor diet, including excess caffeine or sugar	Malnutrition mediated neurological disorders
Poor sleep	Reduced melatonin synthesis and mental imbalance
Sexual abuse	Psychological fears and trauma
Genetic depression and role of candidate genes	Over expression or low expression of candidate genes causing depression
Health issues	Disease induced depression
Perturbations in brain chemistry	Improper brain function induced depression
Rejection and Loneliness	Isolation induced depression
Loss of loved one	Perturbed feelings induced depression
Environmental factors	Physical and chemical factors induced depression

Table 2. A summary of different important remedies implied in depression

Remedies	Actions
Psychotherapy	Maintaining mental and emotional balance
Brain Stimulation Therapies	Activation of inactive or less active brain areas
Cognitive therapy	Restoring memory
Antidepressant medication	Blocking the reuptake of neurotransmitters (serotonin, noradrenaline or dopamine)

identify the thoughts and images that accompany and precede the experience of upsetting emotions, (ii) distance themselves from these thoughts and images, (iii) validate their beliefs and (iv) identify the themes in the content of the thoughts and images that occur across a range of situations.

Chemical treatments

Antidepressant medication: The antidepressant medications include agents that block the reuptake of serotonin, noradrenaline or dopamine, the key players of the neurotransmitter systems. The selective serotonin-reuptake inhibitors (SSRIs) have been the most widely prescribed antidepressant medications to date, although the newer serotonin/noradrenaline-reuptake inhibitors (SNRIs) are also now coming into frequent use. The effectiveness of antidepressant treatment has been proved through several placebo-controlled clinical trials, though different patients respond differently to the antidepressant treatment when used in isolation or in combination of antidepressant treatment [35-37].

However, the antidepressant treatments appear to be symptom-suppressive rather than remedial [38]. It has been observed that the antidepressant treatment decreases future risk of depressive episodes once their use is terminated [39]. Research on humans and animals have indicated that antidepressant treatments may alter the regulatory processes of monoamine systems, especially the serotonin (5-HT), noradrenaline (NA) and dopamine (DA) systems. These agents have been observed to influence the neurotransmitter metabolism for example MAOIs can affect neurotransmitters degradation, the SSRIs, SNRIs, and tricyclic antidepressants (TCAs) can affect the reuptake mechanisms which can reduce appetite, emotional responses, sleep, and sexual interest in the patients suffering from depression [40,41]. A summary of these remedial measures have been presented in Table 2.

Conclusion

In addition to the factors such as abusing drugs and alcohol, overwork, poor diet, use of excess caffeine or sugar, lack of exercise, poor sleep, sexual abuse, genetic disorders, sadness, physical health issue, brain chemistry imbalance, lack of confidence, rejection/loneliness, loss of loved one etc., several environmental factors have been found to associated to trigger depression in an individual. These factors comprise physical, chemical and biological indices. The application of physiological or chemical treatments has proved to act as effective tools towards successful remedies of patients from depression. The cognitive therapy and antidepressant medications have shown effective promises in treating depression. However, extensive research is required to delineate the population suffering from a specific factor which induces depression as it may help develop adequate therapy to treat the patients quickly and effectively.

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Conflicts of interests

The authors declare that they do not have any conflicts of interests.

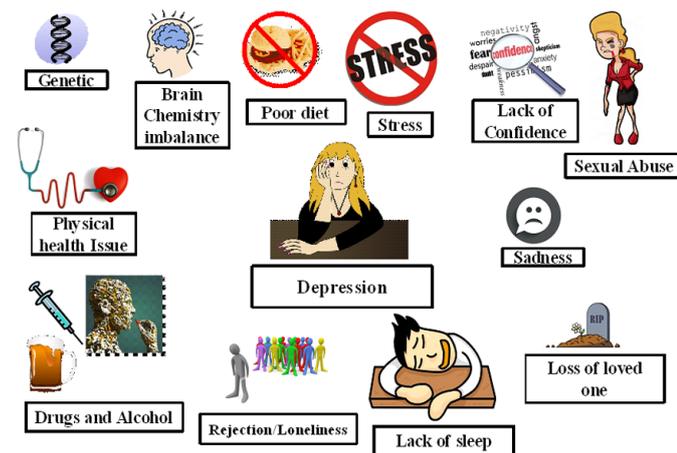


Figure 1. Scheme showing factors responsible for depression

Remedial measures to combat depression

Psychotherapy: Psychotherapy helps by teaching new ways of thinking and behaving, and changing habits that may be contributing to depression. This therapy can help understand and work through difficult relationships or situations that may be causing depression or making it worse.

Brain Stimulation Therapies: Electroconvulsive therapy (ECT) and other brain stimulation therapies may be useful to those people suffering from severe depression who do not respond to antidepressant medications. ECT is considered to be the best therapy with longest history of use.

Physiological treatments

Cognitive therapy: Cognitive therapy has been found to be the most appropriate, safe and efficacious therapy of major depressive disorder. Cognitive therapy provides protection against relapse and recurrence [34]. Cognitive therapy may help patients acquire the abilities to (i)

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