# Major depressive disorder

## Major Depressive Disorder

### Preface

Today, there are so many people suffering from so many diseases. Likewise, so many people started to feel depressed without a reason. Maybe there should be a reason but most people fail to find it and live their life as it goes by.

Now, depressive disorder has become one of major diseases. Boys, girls, teenagers, 20s, 30s, 40s, most people regardless of their age are suffering from major depressive disorder. Because of this, suicidal rate has been increased far more than ever.

Maybe, because of technological revolution, many people started to feel as if they are alone, for people talk through internet, telephone, and so on, they do not feel as if somebody is beside them.

Because of this, I wanted to research on ‘ major depressive disorder’ to figure out what are causing this and what are some ways to prevent this.

### Symptoms and Signs

Major depression is a serious illness that affects a person’s family and personal relationships, work or school life, sleeping and eating habits, and general health. Its impact on functioning and well-being has been equated to that of chronic medical conditions such as diabetes.

A person suffering a major depressive episode usually exhibits a very low mood, which pervades all aspects of life, and an inability to experience pleasure in activities that formerly were enjoyed. Depressed people may be

preoccupied with, or ruminate over, thoughts and feelings of worthlessness, inappropriate guilt or regret, helplessness, hopelessness, and self-hatred. In severe cases, depressed people may have symptoms of psychosis. These symptoms include delusions or, less commonly, hallucinations, usually of an unpleasant nature. Other symptoms of depression include poor concentration and memory (especially in those with melancholic or psychotic features), withdrawal from social situations and activities, reduced sex drive, and thoughts of death or suicide.

Insomnia is common among the depressed. In the typical pattern, a person wakes very early and is unable to get back to sleep. Hypersomnia, or oversleeping, is less common. Appetite often decreases, with resulting weight loss, although increased appetite and weight gain occasionally occur. The person may report multiple physical symptoms such as fatigue, headaches, or digestive problems; physical complaints are the most common presenting problem in developing countries, according to the World Health Organization’s criteria for depression. Family and friends may notice that the person’s behavior is either agitated or lethargic.

Depressed children often display an irritable rather than a depressed mood, and show varying symptoms depending on age and situation. Most exhibit a loss of interest in school and a decline in academic performance. They may be described as clingy, demanding, dependent, or insecure. Diagnosis may be delayed or missed when symptoms are interpreted as normal moodiness. Depression may also coincide with attention-deficit hyperactivity disorder (ADHD), complicating the diagnosis and treatment of both.

Older depressed persons may have cognitive symptoms of recent onset, such as forgetfulness, and a more noticeable slowing of movements. Depression often coexists with physical disorders common among the elderly, such as stroke, other cardiovascular diseases, Parkinson’s disease, and chronic obstructive pulmonary disease.

## Causes

The biopsychosocial model proposes that biological, psychological, and social factors all play a role to varying degrees in causing depression. The diathesis-stress model posits that depression results when a preexisting vulnerability, or diathesis, is activated by stressful life events. The preexisting vulnerability can be either genetic, implying an interaction between nature and nurture, or schematic, resulting from views of the world learned in childhood. These interactive models have gained empirical support. For example, researchers in New Zealand took a prospective approach to studying depression, by documenting over time how depression emerged among an initially normal cohort of people. The researchers concluded that variation among the serotonin transporter (5-HTT) gene affects the chances that people who have dealt with very stressful life events will go on to experience depression. Specifically, depression may follow such events, but seems more likely to appear in people with one or two short alleles of the 5-HTT gene.

A Swedish study estimated the heritability of depression—the degree to which individual differences in occurrence are associated with genetic differences—to be approximately 40% for women and 30% for men, and evolutionary psychologists have proposed that the genetic basis for

depression lies deep in the history of naturally selected adaptations. A substance-induced mood disorder resembling major depression has been causally linked to long-term drug use or abuse, or to withdrawal from certain sedative and hypnotic drugs.

## Biological

### Monoamine hypothesis

Most antidepressant medications increase the levels of one or more of the monoamines—the neurotransmitters serotonin, norepinephrine and dopamine—in the synaptic cleft between neurons in the brain. Some medications affect the monoamine receptors directly.

Serotonin is hypothesized to help regulate other neurotransmitter systems; decreased serotonin activity may allow these systems to act in unusual and erratic ways. According to this “ permissive hypothesis”, depression arises when low serotonin levels promote low levels of norepinephrine, another monoamine neurotransmitter. Some antidepressants enhance the levels of norepinephrine directly, whereas others raise the levels of dopamine, a third monoamine neurotransmitter. These observations gave rise to the monoamine hypothesis of depression. In its contemporary formulation, the monoamine hypothesis postulates that a deficiency of certain neurotransmitters is responsible for the corresponding features of depression: “ Norepinephrine may be related to alertness and energy as well as anxiety, attention, and interest in life; lack of serotonin to anxiety, obsessions, and compulsions; and dopamine to attention, motivation, pleasure, and reward, as well as interest in life.” The proponents of this theory recommend the choice of an antidepressant with mechanism of

action that impacts the most prominent symptoms. Anxious and irritable patients should be treated with SSRIs or norepinephrine reuptake inhibitors, and those experiencing a loss of energy and enjoyment of life with norepinephrine- and dopamine-enhancing drugs.

Schematic of a synapse between an axon of one neuron and a dendrite of another. Synapses are specialized gaps between neurons. Electrical impulses arriving at the axon terminal trigger release of packets of chemical messengers (neurotransmitters), which diffuse across the synaptic cleft to receptors on the adjacent dendrite temporarily affecting the likelihood that an electrical impulse will be triggered in the latter neuron. Once released the neurotransmitter is rapidly metabolised or pumped back into a neuron. Antidepressants influence the overall balance of these processes. In the past two decades, research has revealed multiple limitations of the monoamine hypothesis, and its explanatory inadequacy has been criticized within the psychiatric community. Intensive investigation has failed to find convincing evidence of a primary dysfunction of a specific monoamine system in patients with major depressive disorders. The medications tianeptine and opipramol have long been known to have antidepressant properties despite the fact that the former is a serotonin reuptake enhancer and the latter has no effect on the monoamine system. Experiments with pharmacological agents that cause depletion of monoamines have shown that this depletion does not cause depression in healthy people nor does it worsen symptoms in depressed patients—although an intact monoamine system is necessary for antidepressants to achieve therapeutic effectiveness. According to an essay published by the Public Library of Science (PLoS), the monoamine

hypothesis, already limited, has been further oversimplified when presented to the general public as a mass marketing tool.

## Other theories

MRI scans of patients with depression have reported a number of differences in brain structure compared to those without the illness. Although there is some inconsistency in the results, meta-analyses have shown there is evidence for smaller hippocampal volumes and increased numbers of hyperintensive lesions. Hyperintensities have been associated with patients with a late age of onset, and have led to the development of the theory of vascular depression.

There may be a link between depression and neurogenesis of the hippocampus, a center for both mood and memory. Loss of hippocampal neurons is found in some depressed individuals and correlates with impaired memory and dysthymic mood. Drugs may increase serotonin levels in the brain, stimulating neurogenesis and thus increasing the total mass of the hippocampus. This increase may help to restore mood and memory. Similar relationships have been observed between depression and an area of the anterior cingulate cortex implicated in the modulation of emotional behavior. One of the neurotrophins responsible for neurogenesis is the brain-derived neurotrophic factor (BDNF). The level of BDNF in the blood plasma of depressed subjects is drastically reduced (more than threefold) as compared to the norm. Antidepressant treatment increases the blood level of BDNF. Although decreased plasma BDNF levels have been found in many other disorders, there is some evidence that BDNF is involved in the cause of depression and the mechanism of action of antidepressants.

Major depression may also be caused in part by an overactive hypothalamic-pituitary-adrenal axis (HPA axis) that is similar to the neuro-endocrine response to stress. Investigations reveal increased levels of the hormone cortisol and enlarged pituitary and adrenal glands, suggesting disturbances of the endocrine system may play a role in some psychiatric disorders, including major depression. Oversecretion of corticotropin-releasing hormone from the hypothalamus is thought to drive this, and is implicated in the cognitive and arousal symptoms.

Depression may be related to the same brain mechanisms that control the cycles of sleep and wakefulness. Depression may be related to abnormalities in the circadian rhythm, or biological clock. For example, the REM stage of sleep, the one in which dreaming occurs, may be quick to arrive and intense in depressed people. REM sleep depends on decreased serotonin levels in the brain stem, and is impaired by compounds, such as antidepressants, that increase serotoninergic tone in brain stem structures. Overall, the serotonergic system is least active during sleep and most active during wakefulness. Prolonged wakefulness due to sleep deprivation activates serotonergic neurons, leading to processes similar to the therapeutic effect of antidepressants, such as the selective serotonin reuptake inhibitors (SSRIs). Depressed individuals can exhibit a significant lift in mood after a night of sleep deprivation. SSRIs may directly depend on the increase of central serotonergic neurotransmission for their therapeutic effect, the same system that impacts cycles of sleep and wakefulness.

Research on the effects of light therapy on treating seasonal affective disorder suggests that light deprivation is related to decreased activity in the

serotonergic system and to abnormalities in the sleep cycle, particularly insomnia. Exposure to light also targets the serotonergic system, providing more support for the important role this system may play in depression. Sleep deprivation and light therapy both target the same brain neurotransmitter system and brain areas as antidepressant drugs, and are now used clinically to treat depression. Light therapy, sleep deprivation and sleep time displacement (sleep phase advance therapy) are being used in combination quickly to interrupt a deep depression in hospitalized patients.

The hormone estrogen has been implicated in depressive disorders due to the increase in risk of depressive episodes after puberty, the antenatal period, and reduced rates after menopause. Conversely, the premenstrual and postpartum periods of low estrogen levels are also associated with increased risk. The use of estrogen has been under-researched, and although some small trials show promise in its use to prevent or treat depression, the evidence for its effectiveness is not strong. Estrogen replacement therapy has been shown to be beneficial in improving mood in perimenopause, but it is unclear if it is merely the menopausal symptoms that are being reversed.

Other research has explored potential roles of molecules necessary for overall cellular functioning: cytokines and essential nutrients. The symptoms of major depressive disorder are nearly identical to those of sickness behavior, the response of the body when the immune system is fighting an infection. This raises the possility that depression can result from a maladaptive manifestation of sickness behavior as a result of abnormalities in circulating cytokines. Deficiencies in certain essential dietary nutrients,

particularly vitamin B12 and folic acid, have been associated with depression; other agents such as the elements copper and magnesium, and vitamin A have also been implicated.

## Prevention

A 2008 meta-analysis found that behavioral interventions, such as interpersonal therapy, are effective at preventing new onset depression. Because such interventions appear to be most effective when delivered to individuals or small groups, it has been suggested that they may be able to reach their large target audience most efficiently through the Internet. However, an earlier meta-analysis found preventive programs with a competence-enhancing component to be superior to behaviorally oriented programs overall, and found behavioral programs to be particularly unhelpful for older people, for whom social support programs were uniquely beneficial. Additionally, the programs that best prevented depression comprised more than eight sessions, each lasting between 60 and 90 minutes; were provided by a combination of lay and professional workers; had a high-quality research design; reported attrition rates; and had a well-defined intervention. The “ Coping with Depression” course (CWD) is claimed to be the most successful of psychoeducational interventions for the treatment and prevention of depression (both for its adaptability to various populations and its results), with a risk reduction of 38% in major depression and an efficacy as a treatment comparing favorably to other psychotherapies.

## References

http://en. wikipedia. org/wiki/Depressive_disorder#Prevention