The Possible Biological Effects of Long-term Stress on Depression

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Abstract
Depression is a disorder in which a person is unfit physically and mentally. WHO stated it is the fourth major cause of passing disable life. It reduces individual’s productive life and leads to premature mortality. From last 20 years an extensive research has been done to find relationship between life stress and depression. Stress is not the sole causative factor, but genetic as well as biological changes in the depressed individual play important role in the onset of depression. Other predisposing factors for depression include childhood stress such as ignorance by family, early loss of parents, physical or sexual abuse, no social support, financial loss etc. Stressful life events can lead to depression has been explored by many researchers and concluded that stressful life-events can arouse or trigger depression episodes in susceptible individuals.

Keywords: Stress; Depression; Stressors

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1. Introduction
Depression is one of the most disabling medical disorders. It is characterized by significant physiological changes such as anorexia, constipation, insomnia, fatigue, lethargy, gastrointestinal disturbances, dizziness or other faint body aches. According to WHO, depression is the 4th leading cause of passing life with poor physical and mental health. The productive life of depressed person is decreased and his life moves towards early death [1-2]. Many studies were carried out to explore any relationship between stressful life events and depression [3-8].

2. Types of Depression
There are several types of classifications of depression but more simply it is classified into two types: 1) endogenous depression 2) exogenous depression.

Endogenous depression is characterized by changes in neurotransmitter levels in the synapses while depression aroused because of stress or tension is called exogenous depression [9].

Physical, mental, or emotional response to life events that cause mental tension is called stress. Stress can be caused by:
1) Dependent events such as death of some dear one, separation or threat of separation between very close relations can generate great stress and weak nerve persons cannot cope with it and undergo depression [10].
2) Independent events e.g. widowhood, and exposure to natural Disaster [3]. Onset of depression relies more on dependent events than independent events [10].

3. Risk Factors for Depression
1) External stressors (worse life experiences)
2) Genetic / Familial factors

Although external stressors (anything that induce/cause stress is called stressor) are the

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primary trigger for start of depression episodes but genetic/familial parameters cannot be avoided since the rates of depression are higher among first-degree biological relatives than in the general population [11]. Less social contacts in the family may also trigger depression in genetically predisposed individuals. It has been proved from twin pairs genetic studies that individuals who have family history of depression can quickly develop depression when face stress in their life [12]. Other individuals who do not have such familial or genetic predisposing factors when experienced stress in life, show the symptoms and biological markers of depression. Kendler et al., 1993 have studied direct effects of stressful life events on depression [13]. Chances of depression increase with life problems such as divorce, financial problems, and being a crime victim [10]. Severe life stresses can show characteristics of depression within three to four weeks [14, 15], and can also trigger genetic risk factors that have strong correlation with major depression [16]. Other major risk factors for depression include negligence in early life years, early loss of one or both parents either by separation or death, physical abuse [17].

4. Biological Theories of Depression
Several theories for depression have been proposed. Depression is due to genetic as well as biological changes in depressed individual. Studies of genetics, twin cohorts, and neurotransmitters, over the past 30 years, have given an idea that genetic changes or familial component are the causes of depression. To study neurotransmitters, three different approaches have been used: 1) A deficiency model, 2) An imbalance model, and 3) the systems dysregulation model [18]. According to the deficiency model, the depression was related to the deficiency of norepinephrine (NE), however, the latest theories proposed some complexity in arousal of depression [19]. An imbalance model theory states that depression is due to an imbalance between levels of NE and acetylcholine. Dysregulation model is the most advance theory and according to it the depression is due to dysregulation of cortisol level in the body [18].

5. Stress Theory
Stress theory was coined to prove that there is a mood disturbance in depression which is caused by stress in life. According to a study, depressed patients started to exaggerate their life events at least six months before the onset of depressive episodes as compared to control groups [19]. There are few studies which claimed that social support can help patients to get rid of stress, on the other hand low social support can generate sense of failure or low self-esteem in at risk persons but according to Vilhjalmsson, 1993 [20]; Brown and Harris 1978 [14], there is no clear role of social support in the relationship between stress and depression.

6. Cognitive Theories of Depression
These theories support the hypothesis that hopelessness reflecting the victim's belief that negative events will persist [21]. Seligman suggested that animal models of learned helplessness can present the picture of depression [22].

7. Psychodynamic Perspectives
The psychodynamic perspective concludes that depression is not an organic disease, but it is a defense by the ego against intra-psychic conflict [23]. The core presumptions of this theory include:

1) Depression is mainly due to some early life defect, such as the loss of a parent
2) Bad life experiences such as divorce or loss of a job can provoke depression episodes
3) Helplessness and hopelessness are the major contributing factors to depression
4) Ambivalence toward love objects is fundamental to the emotional issues at hand; 5) Loss of self-esteem is an important feature of depression [23].

8. Methods to Study Relationship Between Stress and Depression
Two methods were used for this study a) life events checklist b) and interview method [14]. However, McQuaid, 2000 [24] and Simons et al., 1993 [25] found that the interview methods are more effective in predicting outcomes (depression) as compared to the interview methods.

9. Clinical Studies Demonstrating the Relationship Between Stress and Depression
Studies reported, based on comparison between control group and research group (depressed patients) suggest that great stress can initiate depressive episodes in patients as compared to the control group [4,26]. Mazure, 1998 reported that the major stressful life events can cause depression in 80% individuals and depressed patients experienced 2.5 times more stress as compared to other study groups [4]. Although stress plays major role to induce depression but there has been found that individual's genetic risk factors also influence major depression episodes [27]. In a clinical study, follow up cases of patients were categorized into three groups; a) medical illness b) bipolar (mood swings in two directions, in this
depression alternates with mania) disorder, and no disorder and were compared with a clinical sample of patients with histories of recurrent unipolar depression. In this research, the term “stress generation” was coined to present the conclusion. It was concluded that recurrent unipolar depression patients had to face extreme stress due to dependent events of life. Therefore, this study proves that the dependent events are more predictive of depression episodes [10]. The relationship between generation of stress and major depression had been explored in various studies, including community samples of late adolescent women [28], adolescent males and females [29-30], adult men [31] and women [32-33], children of depressed mothers [34] and clinical samples of children and adolescents [35-36] and adults [37]. Most of these studies revealed that the elevated rates of stressors among those with depression histories did not occur for independent (fateful) events, and were specific to the dependent events that were especially likely to reflect interpersonal content.

10. Conclusion
Stressful life events can move an individual towards depression. Stressful life events can arouse genetic risk factors that are positively correlated with major depression. It is concluded that risk factors of depression (genetics, early life stress, such as childhood ignorance, early loss of parents, physical or sexual abuse) and ongoing life stresses ultimately lead to depression.

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