# Can Statins Diminish Depression?

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## ABSTRACT

Depression is a common malady associated with numerous chronic medical conditions such as coronary artery disease, hypertension, and diabetes. Statins provide protection against coronary and cerebrovascular diseases by decreasing cholesterol synthesis in the liver. Statin medications also reduce inflammation. Since the pathophysiology of depression involves inflammation, statins could have a role in the treatment of mood disorders and might become a pharmacotherapy option for patients experiencing depression. There is evidence suggesting an antidepressant effect when statins are adjunctively co-prescribed with antidepressant medicines. However, confounding data also exist refuting a positive effect of these drugs at elevating mood. More research is required to confirm a potentially beneficial effect of prescribing statins to people with clinical depression.


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Depressive disorders are the fourth-leading cause of disability worldwide and are expected to become more prevalent by 2020.[1] Depression has been associated with many chronic medical conditions, including coronary artery disease, diabetes mellitus, hypertension, cancer, and asthma—depression is a risk factor for their development and also a sequela of them.[1]

Statin drugs (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) are vital in the primary and secondary prevention of coronary and cerebrovascular diseases. Statin drugs provide protection by decreasing cholesterol synthesis in the liver,[2] which reportedly also has beneficial effects on other conditions such as cancer, multiple sclerosis, dementia, and osteoporosis.[3]

Statin medications also reduce inflammation.[3] The pathophysiology of depression involves inflammation.[3] Thus, statins could have a role in the treatment of people with mood disorders and might become a pharmacotherapy option for patients experiencing depression.

## PATHOGENESIS OF DEPRESSION: INFLAMMATION

The pathophysiology of depression involves inflammation, oxidative stress, nitrosative stress, and other mechanisms. Elevated levels of the inflammatory markers such as C-reactive protein, interleukin (IL)-6, tumor necrosis factor alpha, and IL-1 receptor antagonist are observed in patients with depression, independent of physical illness. These elevations were detected during episodes of depression and also with worsening symptoms of the disease[4]; somatic conditions, which have an underlying inflammatory mechanism, are associated with a higher risk of depression. In patients with malignant melanoma, treatment with interferon alpha (proinflammatory) leads to depression in many cases.[4] When antidepressant drugs were prescribed for such patient populations before interferon treatment, a reduction in symptoms of depression was induced.[4] Thus, inflammation might be an underlying mechanism in the development of mood disorders.

## STATINS AND DEPRESSION

The anti-inflammatory characteristics of statin drugs are under investigation.[5] These medications assist in reduction of C-reactive protein levels, possess antioxidant properties, and restrict expression of proinflammatory cytokines by monocytes.[5] These pharmaceuticals also can help in stabilizing endothelium.[5] The anti-inflammatory properties of statins might be responsible for mood improvements in some people. Statins aid cardiovascular health and quality of life and also may decrease depression. One double-blind trial[6] documented that adding a statin to selective serotonin reuptake inhibitor (SSRI) drug treatments yielded a significantly diminished degree of clinical depression in subjects compared to prescribing an SSRI with a placebo. An investigation[7] that compared simvastatin with fluoxetine versus a placebo with fluoxetine documented that prescribed statins were associated with a faster recovery; yet, remission rates were not significantly different among the groups. These outcomes were reaffirmed in a large population-based study.[8] The combined intervention resulted in a significant reduction in psychiatric hospitalizations for depression and fewer reports of being suicidal.[8]

**Clinical Points**

- Statin drugs can reduce inflammation and may have a role in the pathophysiology of depression, but this hypothesis is not conclusively substantiated in repeated studies.
- In patients with mood disorders, statins may be efficacious in diminishing manifestations of depression.
- Statins may be prescribed as an adjunct therapy with selective serotonin reuptake inhibitor pharmacotherapy for the treatment of depression; this combination sometimes decreases affective symptoms more than antidepressants alone.

Prescription of statin medications can result in a decline in depressive symptoms. In a Swedish study,[9] simvastatin reportedly induced a 7% reduction in the severity of depressive moods. Diminished depression was documented more often in elderly people, especially in elderly women, prescribed a statin.[9] A meta-analysis[3] of 9,187 subjects revealed that statins were associated with a 32% reduction in mood complaints. The odds ratio for developing depression in people prescribed a statin was 0.68.[3] Statins were found to decrease depressive manifestations in those with coronary artery disease.[2] Improvement was noted at 1 year and was independent of the patient's medical status. Statin drugs augmented the benefits of escitalopram in persons undergoing depression treatment.[2]

Use of a statin medication can result in decreased inflammatory markers and reportedly leads to a reduction in depressive symptomatology in some subjects; these manifestations appear to be correlated with one another.[2] Statins also have the potential to lower serum lipid concentrations; however, that feature has no specifically documented antidepressant efficacy. Alteration of cholesterol levels and inflammatory markers are independent of one another, even though they are true unrelated characteristics of this medicinal class of drugs.

In patients with coronary artery disease, statins reduced anxiety, depression, and hostility.[10] Depression is often a sequela of traumatic brain injury. Hyperlipidemia after a traumatic brain injury also may facilitate the development of depression. Patients who underwent a hyperlipidemia intervention with a statin medication experienced a lower risk for depression after a traumatic brain injury than those who did not receive the intervention.[11] Statin medications may induce a neuroprotective action in the hippocampus, which could be linked to depression in traumatic brain injury animal models.[11]

Negative associations between statin medications and mood have also been described, specifically that these pharmaceuticals might contrarily induce depression by decreasing the total body cholesterol level.[12] Statins act by lowering cholesterol levels, which affect serotonin pathways, and might have some influence on mood disorders. Decreased lipid concentrations are also correlated with antisocial personality disorders.[12] Research[13] involving elderly subjects showed that taking statin drugs increased their risk of becoming depressed. Reportedly, violence, antisocial personalities, irritability, depression, paranoia, and homicidal or suicidal tendencies can be induced by statins.[4] A meta-analysis[14] involving 2,105 patients was inconclusive: statins did not yield an effect on the psychological outcomes; however, statins did significantly alleviate depressive mood symptoms.

## CONCLUSION

Inflammation can alter brain-signaling pathways and may lead to depression in people who never complained of depressive symptoms in the past.[15] Statin drugs have anti-inflammatory properties and may diminish depressive symptoms in some people. Despite evidence[2,3,5–11] for diminishing affective symptoms, some studies[12–14] refute these findings, suggesting that statins have no effect on mood. Substantiation of the efficacy of statins for alleviating depression is lacking. Thus, more research about the relationship between statins and mood is awaited.[14]

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