

## Mechanisms linking Mental Health Problems and Cardiac Disease: A Review

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### Abstract

Psychological problems play a critical role in development of cardiovascular disease. Several mechanisms were suggested to explain the association and mechanism of this effect, recently. Knowledge of the mechanisms mediating the association between psychological status and heart disease could help in developing treatments. The effects of mind and mood on the cardiovascular system can be due to behavior related (indirect) mechanisms. In fact, mental problems can lead to some behavioral changes which are associated with cardiovascular disease. On the other hand, it can effect on the cardiovascular system directly by elevating stress hormone levels, heartbeat and blood vessels constriction. Therefore, in this review, majority of mechanisms linking mental health disorders and cardiac disease are represented in these two parts.

**Keywords:** Mental Health; Cardiac Disease; Coronary artery disease; Mechanisms

### Introduction

Mental health related factors play a critical role in the incidence and development of cardiac disease (1, 2). Therefore, high percentage of hospitalized heart patients have some mental disorder symptoms (3). Based on the previous studies, psychological problems are related with adverse cardiac outcomes and recurrent cardiac events (4). In fact, individuals who suffer from mental disorders at the time of hospitalization are two to five times more likely to suffer and die from cardiac disease than those without these problems, independent of traditional and known cardiac risk factors (5, 6). Although past surveys did not firmly link mental health status and heart disease, there's a growing belief that it's an additional risk factor, and maybe even more dangerous than some others (7, 8). Lots of mechanisms were proposed to explain the association and mechanism of this effect, recently. For example, some investigators documented that mental problems or feelings of worthlessness may cause those patients to ignore medication plan and avoid treatment for heart disease (9-11). On the other hand, several studies indicated the effects of mind and mood on the cardiovascular system directly by creating a state of emergency readiness, in which stress hormone levels rise, heartbeat speeds up and blood vessels constrict (12, 13). Thus, published models linking mind with cardiac outcomes include both behavioral and physiologic

components (14). In the present paper, majority of mechanisms linking mental health disorders and cardiac disease are reviewed in these two parts. To generate this review article, a search of major psychology and medical databases were carried out using relevant search terms, including stress, cardiac disease, atherosclerosis, mental disorder. In addition, reviewed cited literature from identified articles were also used to discover additional relevant literature.

### Behavior-related Mechanisms

According to the published studies, mental problems can lead to some behavioral changes which are associated with cardiovascular disease such as exercise or physical activities, smoking, adherence to medications and dietary habits (4, 15).

### Exercise or Physical Activities

Several studies stated that older adults with better mental health status have higher rates of physical activity, as a protective factor for cardiac health. In this regard, a meta-analysis performed by S Ahn et al. suggested a significant correlation between health behavior and exercise in children and students (16) who are mainly exposed to the academic stressors (17). In addition, Steptoe et al. found that dispositional optimism in older individuals was related with physical activity,

independent of multiple relevant covariates, including education, living arrangement, self-rated health, body mass index, age, chronic illnesses, medication count, socioeconomic status, and BMI (2). Finally, evidence clarifies negative consistent associations between sedentary screen time and mental health (18). In an investigation conducted by Stuart J H Biddle and Mavis Asare, physical activity interventions for young people have been shown to have beneficial effects for reduced mental disorders (19). On the other hand, lots of strong evidences are available to demonstrate the relationship between physical activity and cardiac disease. For this reason, exercise is necessary to promote mental health status to reduce cardiovascular disease (20, 21).

### Smoking

Tobacco is the leading global cause for the development of coronary heart disease (22). Also, there is a strong link between smoking and poor mental health, and smokers with mental health disorders tend to be heavier smokers and more dependent (23) since they think that smoking provides mental health benefits (24). Smokers experience irritability, anxiety, and depression when they have not smoked for a while and these feelings are reliably relieved by smoking, thus creating the perception that smoking has psychological benefits, while in fact it is smoking that caused these psychological disturbances in the first place (25). Kelloniemi H et al found that optimistic men and women smoked less and individuals with greater optimism were likely to be categorized as having no lifetime smoking history. Therefore, we can conclude that mental disorders can lead to smoking which is an important risk factor for cardiac disease (26).

### Adherence to Medications

Several studies in recent years provided some evidences of strong covariation of mental problems and medical noncompliance (27, 28). These can suggest the importance of recognizing mentioned disorders as a risk factor for poor outcomes among patients who might be noncompliant to medication and medical advices (29). However, a research on patients undergoing heart transplant for end-stage cardiac disease found that mental health was related with adherence to the post-transplant medication (30). In addition, Swartz et al discovered that violence and severe mental illness can lead to nonadherence to the medication (10). Overall,

positive mental attributes have been associated with improved adherence to medical treatment that is important to cardiovascular health (31).

### Dietary Habits

Having a healthy diet gives your brain and your body the vitamins and minerals required to stay healthy (32). In addition, it can significantly reduce the risk of atherosclerosis and further cardiovascular disease (33). However, healthy eating habits can be difficult to maintain, particularly if you have a mental health problem (34). Evidence linking diet and mental health is growing at a rapid pace. Individuals who report some level of mental health problem usually eat fewer healthy foods (fresh fruit and vegetables, organic foods and meals made from scratch) and more unhealthy foods (chips and crisps, chocolate, ready meals and takeaways) (35, 36). In compliance to the literature, in a cross-sectional investigation carried out by Jack et al., some evidences were in a favor of an association between an unhealthy diet and mental health problems (37). Indeed, participants with greater psychological status consumed a greater quantity of vegetables, fruits and high-fiber foods, and a smaller quantity of coffee, alcohol and candy (38). Similarly, Clark et al documented that cases with severe mental illnesses have the unhealthier dietary habits in comparison with normal subjects (39). In conclusion, a balanced mood and mental status can be protected by ensuring that our diet provides adequate amounts of complex carbohydrates, essential fats, amino acids, vitamins, minerals and water (40).

### Physiological Mechanisms

As mentioned, in addition to the behavioral mechanisms, some physiologic pathways were also diagnosed in recent years to justify the adverse effects of psychological disorders on cardiovascular status. In fact, mental health-related pathways have been directly involved in the pathophysiology and treatment of cardiac disease (41, 42). For instance, autonomic nervous system and endothelial dysfunctions, inflammation and increased platelet activity were detected as the major physiological pathways of mental illnesses in cardiovascular disease (43).

### Autonomic Dysfunction

Based on several reports, mental health problems are associated with alteration of cardiac autonomic tone towards decreased parasympathetic activity (44) and an increased sympathetic activity (45). As the heart is innervated by nerves from both the sympathetic and parasympathetic nervous systems, the interplay between these 2 opposing forces helps the heart make changes in response to stressors and other environmental factors (46). Therefore, this alteration can be a logical reason for adverse cardiac autonomic changes in the psychological illnesses. This pattern of autonomic dysfunction has been related with increased mortality in patients with coronary heart disease (47). In this regard, a similar pattern of autonomic dysfunction was observed in animal studies (47, 48). However, cardiac autonomic involvement in mental disorders remains controversial due to methodological issues. In addition to its influences on the heart, autonomic dysfunction may have a negative impact on the vasculature, including the coronary arteries (49). Eventually, we can conclude that various mental health problems can lead to destructive impacts on the functions of autonomic nervous system all of which could lead to vasoconstriction, hypertension, arrhythmia and poor cardiac outcomes (50).

### Endothelial Dysfunctions

The healthy endothelium is a monolayer of cells covering the inner surface of blood vessels, and it acts as a structural and functional barrier between blood and the vessel wall, controlling permeability to plasma components, preventing platelet and leukocyte adhesion and aggregation, and modulating blood flow (51). Therefore, the vascular endothelium performs universal roles in the circulation that include participation in thrombolytic control and thrombosis, vascular growth, vasomotor tone and platelet interactions with the vascular wall (52). Recent studies showed that arterial endothelial function is significantly impaired in patients with mental health disorders (53, 54). In this regard, Rajagopalan et al. measured arterial endothelial function by measurement of brachial artery flow mediated dilatation (FMD) and found the similar results. They suggested that the abnormality persists despite a satisfactory clinical response to antidepressants. However, the main reason of impaired FMD in these individuals is not known (55). On the other hand, endothelial injury in response to various pathological factors leads to inconstancy in the endothelial cell's regulatory functions and the

endothelium becomes incapable of maintaining vascular homeostasis. This abnormality may be a major mechanism by which mental disorders increase the risk of coronary heart disease (56). In fact, endothelial dysfunction appears to play a pathogenic role in the initial development of atherosclerosis (57). In accordance to the above explanations, Broadley et al. documented that arterial endothelial function is impaired in patients with treated depression. Also, they stated that this anomaly may contribute to the elevated risk of cardiac disease observed in depression (58).

### Inflammation

The role of inflammation in the development and progression of a variety of cardiovascular conditions, most notably congestive heart failure and coronary atherosclerosis is well-documented and inflammation is widely considered to be major contributing parameter for the cardiac disease (59). Several numbers of inflammatory cytokines have been related with atherosclerotic plaque formation and progression. These are the main contributors to the pathogenesis of cardiac disease (60). Among the known cytokines, circulating levels of IL-1 are identified with the presence of traditional cardiovascular risk factors, including smoking, hypertension, diabetes mellitus, and dyslipidemia (61). On the other hand, elevated levels of IL-1 can lead to secretion of other cytokines such as IL-6 (60). Increased levels of these cytokines result in activation of endothelial, expression of adhesion molecules, increased vascular permeability, smooth muscle cell proliferation and macrophage activation. Consequently, this cascade promotes atherosclerosis and also plaque destabilization (62, 63). Furthermore, high levels of C-reactive protein (CRP), an acute-phase protein, usually indicated the presence of inflammation in the body (64). In fact, the body creates CRP during the common process of inflammation and thus, this is a marker for inflammation. However, it appears to be associated with the risk of cardiac disease, meaning its presence demonstrates an increased risk of cardiovascular impairments (65). The exact mechanisms by which CRP may lead to the pathogenesis of heart disease are poorly identified. However, the effect of CRP on atherogenesis may include interactions with the immunity and inflammation factors, including the complement system. In addition, it has a direct influence on the cells involved in atherosclerotic lesions (66). On the other hand, Shelton and Miller

indicated that individuals with mental problems exhibit elevated inflammatory markers. They suggested that the inflammatory molecules have high values in depressed patients since these cytokines access the brain and affect neurotransmitter systems relevant to depression (67). The correlation between inflammation and mental health problems was approved by frequent surveys. Therefore, in conclusion, patients with psychological disturbances have higher degrees of inflammation and risk of heart disease, subsequently (68, 69).

### Platelet Activity and Aggregation

Although platelets are important in normal haemostasis, recent evidence emphasises the fundamental role of abnormal platelet function in various coronary artery diseases. Indeed, platelet hyperaggregability, which commonly occurs due to increased pro-aggregatory stimuli or by diminished anti-aggregatory substances, is mainly correlated with the incidence of coronary artery disease (70). Elevated platelet aggregation, lower the threshold for myocardial ischemia, and increases the risk of coronary thrombosis. Interestingly, some authors found that depressed subjects revealed significantly greater platelet activation and responsiveness than did healthy, nondepressed individuals (71). According to the findings of these investigations, plasma concentrations of two proteins (platelet factor 4 and  $\beta$  thromboglobulin) that are produced and secreted from alpha granules when the platelet is activated, were higher in depressed patients with cardiovascular disease than in healthy, nondepressed subjects, and in nondepressed patients with cardiovascular disease (72). Several mechanisms were proposed to explain the interaction between elevated platelet activity and aggregation with mental status in subjects. In this regard, Serotonin, as a substance often implicated in the pathogenesis of depression can bind with 5-hydroxytryptamine receptors on platelets and play a key role in the activation of the platelets and formation of myocardial ischemia (73, 74). The other term in patients with mental disease is platelet dysfunction, meaning abnormalities in blood and platelet serotonin levels, elevated platelet serotonin receptor and abnormally low platelet serotonin transporter levels (75, 76). These alterations make the platelets both more sensitive to serotonin and less able to remove it from the blood. Thus, platelet aggregation linked with mental disorder may

contribute to coronary thrombosis and further cardiovascular disease (77).

### Conclusion

In this review, majority of the plausible ways in which mental factors could have an adverse effect on cardiac functioning and coronary disease were explained. Knowledge of the mechanisms mediating the link between mental status and cardiac disease is important and relatively neglected area for researchers and it could help to improve present treatments and develop new treatments. However, since we still do not know which of the possibilities reviewed here, if any, explain this correlation, further studies and meta analysis on all issues associated with understanding and treating mental problems in cardiac patients are required to approve the clinical manifestation of each mechanism. In addition, evaluation of the efficacy of antidepressant medications in patients with heart disease would be useful to ensure their safety and efficacy in those populations. Finally depending on the explanations in present paper, the identification and treatment of psychological disorders in patients with cardiac disease is recommended as a part of routine care in cardiac patients.

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### Conflict of Interest

The authors declare that they have no conflict of interests.

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