A long history of anecdotal reports links situational stressors to illness and particular attention has been paid to the association between acute psychological stress and cardiovascular disease. More recently, this evidence has been confirmed in epidemiologic and laboratory studies. Epidemiologic studies have shown that death rates in the general population rise after natural disasters. Examples of this observation include increases in acute MI rates in Israel after Scud missile attacks during the Gulf War, increased deaths following the Athens earthquake of 1981, increased defibrillator firings and hospitalizations for MI following the Northridge earthquakes of 1994 and increased cardiac arrhythmic events following the simultaneous terrorist attacks on the World Trade Center and Pentagon in 2001. There is also data that the risk of Myocardial Infarction (MI) is more than 10 times greater in the hour after an episode of intense anger.

In this short review, we will discuss the evidence and mechanisms underlying mental stress-induced myocardial ischemia.

Mental Stress-induced Myocardial Ischemia

Acute mental stress is easier to model in the laboratory than chronic stress and as such a growing body of literature started to lay a foundation for understanding the pathophysiologic mechanisms underlying its association with CAD. It has been suggested that 40 to 70% of patients with CAD experience transient myocardial ischemia in response to acute mental stress. The development of myocardial ischemia in this setting has been shown to confer increased risk for fatal and non-fatal cardiac events, independent of other traditional risk factors.

The majority of patients who develop mental stress-induced myocardial ischemia report no anginal symptoms during the event. Additionally the electrocardiographic changes typically associated with exercise or pharmacologic stress induced ischemia are not usually observed in this situation. Nonetheless, evidence of mental stress ischemia is observed in both laboratory and daily life settings. In fact, ambulatory electrocardiogram (ECG) studies suggest that there may be as much as a three-fold increase in the relative risk of ischemia in the hour following highly negative emotional states. Furthermore, studies suggest that ischemia during daily life follows a circadian pattern. In a study by Krantz and colleagues, a circadian variability in ischemia was observed with a peak at 6 AM. A significant increase in ischemia occurred immediately after awakening, but activity-adjusted increases in morning ischemia persisted for 2 hours afterwards. Furthermore exogenous factors (including mental activities) were found to be the most potent triggers of ischemia during the morning hours.

Mechanisms

Several unique mechanisms seem to be involved in the development of mental stress-induced myocardial ischemia. These will be discussed here under three categories: vascular, coagulation/platelet activation and inflammation:

1. Vascular Mechanisms

Several vascular mechanisms seem to be operative in mental stress-induced myocardial ischemia. Mental stress induces large increases in blood pressure with less dramatic increases in HR. This is mostly due to the fact that mental stress causes pure adrenergic stimulation with lack of parasympathetic withdrawal. Laboratory studies have shown that mental stress induces a rapid rise in systemic vascular resistance with consequent myocardial supply-demand related ischemia. Mental stress has also been shown to induce transient epicardial coronary vasoconstriction. This seems to occur via an endothelium-dependant mechanism. Dakak and associates reported that, the coronary microcirculation fails to dilate during mental stress. Another study found that mental stress blunts the augmentation
of myocardial blood flow in regions without significant epicardial stenosis, suggesting a prominent role for microvascular dysfunction in this setting.  

Rozanski et al suggested that the mechanisms underlying mental stress-induced myocardial ischemia seem to be related to the acute presentation of the stressor, while, for example, response to exercise is usually gradual; a mentally challenging task provides a sudden stressor without a warm-up period.  

2. Platelet/Coagulation Dysfunction during Mental Stress  

A large body of literature has consistently shown that acute psychological stress induces significant increases in coagulant factors and platelet activity and promotes a decrease in plasma volume with consequent hemocoagulation and increased plasma viscosity.  

Platelet activation is one of the intriguing mechanisms that could potentially explain the relationship between acute mental stress and ischemic cardiac events.  

More direct evidence for the role of platelet activation in mental stress-induced ischemic events comes from a recent study by Strike and colleagues who found that patients who had an emotionally triggered acute coronary syndrome exhibited increased platelet reactivity to standard behavioral stress protocols as compared to patients who did not have an emotionally triggered event.  

Hemoconcentration through mental stress-induced decrease in plasma volume with consequent increase in plasma viscosity has also been consistently reported.  

Markers of platelet/coagulation activity such as Von Willebrand factor antigen, factor VIII coagulant activity, thromboxane B2 levels in plasma and serum as well as platelet aggregation markers have all been found to increase significantly in response to mental stress.  

The literature pertaining to the duration of mental stress-induced prothrombotic changes is equivocal. While some studies suggested that these effects are short lasting, others found that they may last up to 4 to 6 months.  

3. Mental stress and inflammatory changes  

It is well documented that cytokines and other inflammatory responses can be triggered by psychological stress. Increased production of pro-inflammatory cytokines such as TNF-α, IL-1β, IL-6, IL-1 Ra, IFN-γ and IL-10 have been observed with laboratory-induced and daily life stressors. Although these findings have not been directly confirmed in patients with CAD, cytokines are known to affect the progression of coronary artery disease. They are thought to enhance atherogenesis and have been linked to cardiac events in this population.

REFERENCES


