

Mental stress reduces blood flow to the heart in patients with gene variation

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University of Florida researchers have identified a gene variation in heart disease patients who appear especially vulnerable to the physical effects of mental stress — to the point where blood flow to the heart is greatly reduced.

“Searching for the presence of this gene may be one way to better identify patients who are at an increased risk for the phenomenon,” said David S. Sheps, M.D., a professor and associate chairman of cardiovascular medicine at UF’s College of Medicine and the Malcom Randall Veterans Affairs Medical Center.

Those with the gene variation are three times more likely to experience dangerous decreases in blood flow to the heart — a condition doctors call ischemia — than heart disease patients without it. Ischemia increases the chance these patients will suffer a heart attack, heart rhythm abnormalities or sudden death, UF researchers report in the April 14 issue of *Archives of Internal Medicine*.

“There’s no question that in certain populations it is associated with worse prognosis than in patients who do not have mental stress-induced ischemia in terms of overall adverse events and also mortality,” Sheps said. “And it has become apparent that it is far more prevalent than we initially thought. Most of the studies that have been published to date have involved populations of patients who had coronary disease and positive exercise stress tests. But recently we and other investigators have shown that a much broader category of patients also are prone to

mental stress ischemia.”

Past studies have shown that as many as two-thirds of patients with coronary artery disease who experience exercise-related reductions in blood flow to the heart respond similarly to mental stress. These bouts often produce no symptoms of chest pain and are rarely detectable on a standard electrocardiogram. Yet previous UF research has shown that these patients have a threefold greater risk of dying — as large a risk factor as cigarette smoking or high cholesterol. Other studies have linked stress experienced after mass disasters or natural catastrophes with a rise in heart attacks and sudden death.

Psychological stress can leave the heart more prone to developing arrhythmias or electrical instability and the blood more prone to clotting. Stress appears to raise heart rate and rapidly hike blood pressure, increasing the heart’s need for oxygen-rich blood, Sheps said. Yet less oxygen is supplied, in part because coronary arteries constrict, impeding blood flow. Doctors are concerned that this reaction to stress in the laboratory is simply a snapshot of how patients respond to the stress of life on a daily basis.

An estimated 10 percent of all patients with coronary disease experience detectable mental stress-induced reductions in blood flow to the heart. In some subsets of patients the phenomenon may be even more prevalent, involving up to 40 percent of these patients.

UF researchers studied 148 patients with coronary artery disease who were on average about 65 years old. Participants were asked to perform a public speaking test designed to induce stress. Images were taken of blood flow to the heart at rest and during the speech task. Blood samples also were collected and analyzed for five common gene variations.

About a fourth of the patients experienced mental stress-induced

reduced blood flow to the heart, and about two-thirds of them harbored a particular variation of the adrenergic beta-1 receptor genotype that was associated with a three-fold increased risk of this phenomenon, said Mustafa Hassan, M.D., the study's lead author and a research fellow in UF's division of cardiovascular medicine. This receptor typically helps the body respond to stress by regulating blood pressure and heart rate, but a common variability in its gene may make certain patients more vulnerable to the effects of psychological stress.

The study was funded by the National Heart, Lung and Blood Institute and also was supported by the Department of Veterans Affairs Medical Center and the UF colleges of Pharmacy and Dentistry.

Why does mental stress restrict blood flow in some patients even when exercise fails to have the same effect? The effects of mental stress could predominantly affect the heart's smaller vessels, causing them to spasm and temporarily limiting blood flow, Sheps speculated. In contrast, exercise tends to affect the heart's blood supply through different mechanisms.

"We should focus our research on two areas," he said. "One is better identification of patients who are prone to have this problem and two is looking for effective treatments once we know they have it. We need to know whether we can reverse this phenomenon. We are embarking on other treatment studies fairly soon."

UF researchers are hunting for other genetic subtypes that could identify other patients at increased risk, he added.

"One of the advantages of detecting these sorts of things is that we may be able to in the future be more specific about what kind of treatment might work better in certain patients depending on their genetic makeup," Sheps said. "That is one of the important things happening in

many fields of medicine. There are many diseases that already have been shown to respond differently to different types of treatment based on genetic differences.”

Source: University of Florida

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