

## Do We Need a Routine Mental Stress Test for Ischemic Heart Disease and Arrhythmias?

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**T**he effect of mental activity on the cardiovascular system has been well known since ancient times. Hippocrates had already observed that "... fear, intimidation, sorrow, anger ..." may lead to palpitations.<sup>1</sup> In his initial report on a "disorder of the breast" William Heberden mentions a "disturbance of the mind" among other incidents triggering angina pectoris attacks.<sup>2</sup> Recent data provide evidence that mental stress may trigger the appearance of ischemic attacks or arrhythmias.

### Mental stress and myocardial ischemia

Ischemia has been documented in otherwise healthy individuals, and more often in patients with coronary heart disease, following anger, public speaking, driving problems, job stress, while watching competitive sports (soccer), or after natural disasters, wartime incidents, during depression, etc.<sup>3-5</sup> The relative risk for myocardial infarction rose to 2.3-9 during the first hour after feeling very angry,<sup>3</sup> while only 4-7% of infarctions follow physical exercise.<sup>6</sup> Mental stress lowers the threshold of work and heart rate at which ischemia appears during physical exercise.

It is estimated that approximately 25% of ischemic attacks are precipitated by mental stress and 83% of them are silent.<sup>7</sup> Positive electrocardiographic signs were seen in 9 out of 29 patients with a negative exercise test.<sup>8</sup> Ischemic symptoms were reported in

firefighters more often while they were rushing to a fire or returning from it (32.1% and 32.8%, respectively) than during physical training (12.5%). Sequential rest and anger periods in a mental stress protocol were found to increase the risk of myocardial ischemia in patients with stable angina. Extreme stress conditions may cause myocardial necrosis.

More recently, markers of inflammation related to ischemic attacks, such as C-reactive protein, interleukin-6 and soluble intercellular adhesion molecule 1, were found to increase, not only with treadmill exercise, but also following mental challenge tests such as mental arithmetic, or anger recall.<sup>9</sup>

Brain activity has been found to relate to stress in patients with coronary heart disease. In positive emission tomography scans, excessive metabolic activity in the left parietal lobe and other parts of the brain was seen during mental stress in coronary patients but not in healthy individuals. Brain lesions in strokes are accompanied by ischemic myocardial signs in 25% of cases.<sup>10</sup>

Many mechanisms are known that connect mental stress and ischemic events. Mental stress may be followed by increased oxygen demand, spasms of the coronary vessels (especially if other lesions already exist), repolarization changes,<sup>11</sup> elevated catecholamines and cortisol,<sup>12</sup> endothelial dysfunction,<sup>13</sup> elevated blood cholesterol and low HDL, increased platelet activity, etc.<sup>14</sup>

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## Mental stress and cardiac arrhythmias

Mental stress can trigger arrhythmias, especially in patients with preexisting myocardial ischemia. In patients with implanted defibrillators 15% of ventricular arrhythmias are preceded by an elevated level of anger.<sup>15</sup> Idiopathic ventricular fibrillation was preceded more often by psychological stress in the previous 24 hours than in the previous 6 months.<sup>16</sup> In patients with implantable defibrillators ventricular tachycardia or fibrillation was twice as likely to occur within one hour of driving a car.<sup>17</sup> Again, in patients with implantable defibrillators ventricular arrhythmias were induced by mental stress in coronary heart disease.<sup>15</sup> Electrical instability of the ventricles, as assessed by T-wave *alternans*, in patients with implanted defibrillators was observed at lower heart rates following mental stress than during physical exercise.<sup>18</sup>

Other findings suggest a relationship between arrhythmias and the activity of the central as well as the autonomic nervous system.<sup>19</sup> The ventricular fibrillation threshold can be lowered by stimulating the lateral and posterior hypothalamus. Activation of the hypothalamic-adrenal axis increases myocardial excitability. Shorter refractory periods are seen during sympathetic stimulation. In addition, electrical instability leading to arrhythmias may result from inhomogeneous stimulation of the myocardium by sympathetic neurons reaching the ventricles.

Cardioneuropathy is an entity in which limbic regions of the brain may induce abnormal firing properties of affected neurons. Areas of hypersensitivity in the heart may then trigger arrhythmias. Repolarization changes were seen in patients with coronary heart disease, but not in controls, following mental stress. Interestingly, mechanisms for mental stress-induced arrhythmias may involve autonomic pathways that differ from those in exercise-induced arrhythmias. Experimental evidence indicates that ventricular arrhythmias triggered by pressure changes may be prevented by b-adrenergic blockade.<sup>20</sup>

Serious arrhythmias may be the cause of a number of sudden deaths in patients with no atheroma rupture or thrombi occluding a coronary artery found at *post mortem* examination. In fact no pathologic lesions are found in 5% of sudden death cases. Arrhythmias caused by any of the above described mechanisms may be responsible.

### The need for a mental stress test

In spite of data indicating that a percentage of sudden

ischemic events or arrhythmias are triggered by mental stress in patients with heart disease, as well as in some apparently healthy individuals, there is no widely applied method to evaluate the importance of this mechanism, in contrast to all the efforts to quantify physical exercise.

The need for a routinely applied mental stress test is obvious, at least in patients with coronary heart disease or arrhythmias. The practical purpose of such a test would be diagnostic in both ischemic heart disease and arrhythmias. In ischemic conditions it would complement the exercise test by possibly revealing the existence of other injurious factors, apart from physical exercise, that might trigger the events. It could also reveal the existence of coronary heart disease in a number of patients with a normal ECG both at rest and during exercise. In arrhythmias it would serve to indicate the degree of the nervous system's contribution to the causative or precipitating mechanisms.

Standardizing a protocol for mental stress testing will be more difficult than it was for the exercise test. In previous studies several protocols were used, involving mental arithmetic with oral or written response, with or without superimposed noise distractions, or various types of challenges, anger recall interviews, simulated public speaking, Stroop color-word task etc.<sup>21-23</sup> Trials of several tests in large numbers of patients will be necessary before one or more protocols are adopted for routine use. One must remember, however, that Master's first paper on the importance of an exercise test was published in 1934,<sup>24</sup> whereas the protocol most used today was proposed in 1963.<sup>25</sup>

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