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Hypoxia training suppresses harmful cardiac nitric oxide production during heart attack

Intermittent hypoxia minimizes harmful nitric oxide formation in canine heart subjected to coronary occlusion and reperfusion

Researchers at the University of North Texas Health Science Center, Fort Worth, Texas have demonstrated that, contrary to prevailing dogma, hypoxia can be remarkably beneficial to the heart. These discoveries, to be reported in the June 2008 issue of Experimental Biology and Medicine, may lead to a new paradigm to protect hearts of patients at risk of coronary disease. Hypoxia is generally considered harmful to the heart, since a steady supply of oxygen is required to maintain cardiac function. However, this research has demonstrated that a 20 day program of brief, repetitive, moderate reductions in the amount of oxygen in the arterial blood induce adaptations which increase the heart's resistance to the more severe insult of a heart attack. In particular, intermittent hypoxic treatment of dogs remarkably reduced myocardial infarction and lethal arrhythmias following coronary artery occlusion and reperfusion.

The research team, led by Robert T. Mallet, Associate Professor of Integrative Physiology, H. Fred Downey, Regents Professor of Integrative Physiology, and doctoral student Myoung-Gwi Ryou explored mechanisms that may be responsible for this remarkable cardioprotection. Specifically, the investigators tested the hypothesis that intermittent hypoxia treatment suppressed harmful over-production of nitric oxide, the precursor of a host of toxic compounds, by heart tissue upon coronary artery reperfusion. One day after completing 20 days of intermittent hypoxia treatment, dogs were anesthetized and a coronary artery was surgically obstructed for 60 minutes, and then the obstruction was removed and artery was reperfused. An explosive burst of cardiac nitric oxide production occurred during the first few minutes of reperfusion in untreated dogs, but this harmful burst was considerably dampened in hypoxia-treated dogs, without compromising recovery of coronary blood flow. Hypoxia treatment also suppressed cardiac activity of nitric oxide synthase (NOS), the enzyme that

produces nitric oxide, as well as the heart's content of the principal NOS isoform, endothelial NOS.

According to Dr. Mallet, reduced NOS activity may contribute to the cardiac benefits of hypoxia treatment by decreasing formation of a free radical, superoxide, as well as nitric oxide. Both of these compounds are produced by NOS. When these two compounds are produced simultaneously, they combine to form peroxynitrite, an extremely aggressive chemical by-product that injures the heart by damaging the molecular components of cells. By decreasing NOS activity in the heart, hypoxia treatment could minimize formation of peroxynitrite and other harmful products of nitric oxide and superoxide.

Intermittent hypoxia treatment may be a powerful adjunctive therapy for patients at risk of heart disease says Dr. Downey. The brief periods of moderate hypoxia are easily tolerated by most people, require neither surgery nor expensive medications, and can be administered by the patient at home or work using available devices. Indeed, intermittent hypoxia has been used for several decades in Eastern Europe to treat heart and neurological diseases and high blood pressure." Dr. Steven R. Goodman, Editor-in-Chief of Experimental Biology and Medicine stated This study by Robert Mallet and colleagues may suggest a simple treatment to minimize the impact of a heart attack and should stimulate further study of this phenomena"

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