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Rhythm of the Heart

Julie O'Connor Wayne State University

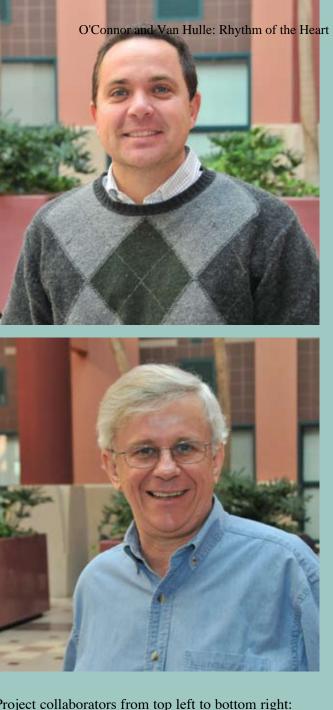
Phillip Van Hulle *Wayne State University*

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Project collaborators from top left to bottom right: Noreen Rossi, M.D., Javier Sala-Mercado, M.D., Ph.D., and Tadeusz Scislo, M.D., Ph.D.

Rhythm of

by Julie O'Connor and Philip Van Hulle

Heart failure is the leading killer of men and women in the United States, according to the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH). When blood flow to a section of the heart muscle decreases or becomes blocked, the heart is deprived of oxygen and begins to die.

Oxygen demand by muscles like the heart during exercise is many times greater than during a resting state. This increased oxygen delivery is accomplished by increased cardiac output and redistribution of blood flow to skeletal muscles. Exercise presents one of the greatest challenges to cardiovascular control, a challenge exacerbated in subjects with cardiovascular diseases such as heart failure and hypertension, often leading to coronary ischemia, impaired ventricular function, arrhythmias and even sudden cardiac death. A team of researchers at Wayne State led by Donal O'Leary, Ph.D., professor of physiology in WSU's School of Medicine, is investigating what causes the reduction of blood flow to muscles and the heart during exercise in patients who suffer from heart failure.

A hallmark feature of heart failure is decreased exercise tolerance, the team noted. "Even under normal circumstances, whole body dynamic exercise is one of the greatest stresses to the cardiovascular system," said O'Leary. "The heartbeat races and blood flow to inactive areas shuts down. With the compromised performance of the heart, even blood flow to the muscles – including the heart itself – is limited."

The cause of these abnormal responses to exercise in heart failure is unknown. Through this research, O'Leary and his collaborators, including Javier

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the heart

Sala-Mercado, M.D., Ph.D., assistant professor of physiology and the Cardiovascular Research Institute; Tadeusz Scislo, M.D., Ph.D., associate professor of physiology; and Noreen Rossi, M.D., professor of Internal Medicine, will investigate the potential role of reflexes arising from the muscles as well as reflexes regulating blood pressure in mediating the extreme responses to dynamic exercise seen in subjects with heart failure.

Dynamic exercise in heart failure patients often brings on profound increases in sympathetic nerve activity that can elicit vasoconstriction, or narrowing of the blood vessels, of the coronary circulation as well as the active skeletal muscle, explained O'Leary. His research aims to determine the roles of the muscle metaboreflex and arterial baroreflex in this altered control of integrative cardiovascular function during exercise in heart failure and the functional consequences of the heightened sympathetic tone on ventricular function and skeletal muscle blood flow.

"It is well known that exercise can have extreme responses to heart failure; however, how these responses occur remains unclear," said O'Leary. "Our objective is to shed new light on the mechanisms responsible for these responses, which is the first step in identifying treatment regimens."

The ultimate goal of this research, funded by the National Institute of Heart, Lung and Blood of the NIH through the American Recovery and Reinvestment Act (ARRA) of 2009, is to provide compelling new information on the altered mechanisms of cardiovascular control during exercise in heart failure. In a second study, also funded by NIH through ARRA, O'Leary will analyze abnormal responses to exercise in patients with well-established hypertension.

Hypertension, or high blood pressure, affects nearly 1 in 3 adults in the United States, and is a major factor for a broad range of cardiovascular diseases, including stroke, congestive heart failure and renal disease. These patients have abnormally large increases in arterial pressure and heart rate in response to exercise, often leading to sudden, adverse cardiovascular events such as myocardial infarction and stroke. Unfortunately, there is little understanding of the mechanisms mediating these abnormal cardiovascular responses to exercise in patients with hypertension.

Through powerful and innovative models, O'Leary and his colleagues hope to uncover information on the effects of hypertension on cardiovascular responses to exercise, ultimately resulting in aiding exercise regimes for hypertensive patients, as well as increasing the understanding of the impact of hypertension on neural control of circulation during one of the greatest challenges to cardiovascular control.

A third project, also funded by the NIH, investigates the role of adenosine as a neuromodulator in the area of the brainstem that integrates sensory information from the cardiovascular system and is ultimately important in control of autonomic nerve activity. "Adenosine levels in the brainstem increase in extreme stressful situations such as the 'fight or flight' defense response, severe hemorrhage, very low oxygen



About Dr. Donal O'Leary:

Dr. O'Leary is professor of physiology and director of cardiovascular research in the Department of Physiology. He received his B.A. in zoology and chemistry from Miami University (Ohio) in 1980 and his Ph.D. in physiology from the University of Texas Health Science Center in San Antonio in 1986. He joined Wayne State in 1989.

levels, high G stress maneuvers such as those done by Air Force pilots in very high performance aircraft – real life or death situations," said O'Leary. His team is investigating how adenosine is involved in the overall integration of central neural control of the cardiovascular system and how this is differentially regulated to different parts of the body.

"Ultimately, our success is due mainly to the outstanding team we have developed over the last two decades here at Wayne State," said O'Leary. "Without this teamwork, these studies would not be possible."

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