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# Trial looks at whether compound relieves cognitive deficits after bypass

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University of Arizona researchers are collaborating on a Phase 2 trial to determine whether a particular peptide administered before and after coronary bypass surgery mitigates or even reverses cognitive deficits thought to be connected to the procedure.

The peptide, known as angiotensin 1-7, a derivative of angiotensin 2, is a naturally occurring compound that relaxes vascular tone, diminishes the dilation of blood vessels, decreases inflammation and is considered safe in normal amounts.

Some patients have a profound response to this procedure, others a minor one.

"After bypass surgery, some people tell us that they feel different, they think differently, and things have changed for them even though their heart is better," says Dr. Nancy Sweitzer, director of the University of Arizona Sarver Heart Center and chief of cardiology in the UA College of Medicine - Tucson.

Some people don't notice anything all. Studies have shown, however, that if cognition and memory are carefully evaluated, tests detect cognitive deficits in a substantial number of people after bypass surgery, says Sweitzer, an expert in heart failure.

"Our body makes angiotensin, which is cleaved to angiotensin 2," says collaborator Meredith Hay, professor of physiology at the UA College of

Medicine - Tucson.

Angiotensin 2 is involved in the body's water balance, an important matter. Many patients with high blood pressure have too much angiotensin 2. However, our bodies have the ability to break down angiotensin 2 into angiotensin 1-7.

The UA researchers are just beginning the trial, which includes patients who come to Banner - University Medical Center Tucson in need of bypass surgery. Last month, the researchers enrolled their first participant.

Hay; John Konhilas, UA associate professor of physiology; and Carol Barnes, director of the UA Evelyn F. McKnight Brain Institute and Regents' Professor of Psychology, previously conducted preclinical studies in mice with heart failure that laid the foundation for the human trial. These pivotal studies showed that angiotensin 1-7 reversed memory loss in mice with heart failure.

Researchers know that when patients have cognitive impairment, it can significantly affect the quality of their health, says collaborator Lee Ryan, a UA clinical neuropsychologist and expert in neuroimaging and the aging brain. Ryan is heading up the study's cognitive testing and brain imaging.

In the double-blind, clinical trial, participants will be given angiotensin 1-7 or a placebo two hours before bypass surgery and will take the drug or placebo every day for 21 days thereafter.

"The drug has got to be onboard and dispersed throughout the body before the patient goes on cardiopulmonary bypass," notes Dr. David Bull, chief of cardiothoracic surgery in the UA College of Medicine - Tucson. Bull and Dr. Zain Khalpey, associate professor of surgery at the

UA College of Medicine - Tucson, are the partner surgeons in the Phase 2 study.

Participants will undergo a series of tests to evaluate their memory before surgery and periodically following surgery, with the last test administered one year after bypass. Imaging of the brain with MRI scans also will take place before and after surgery.

"We don't know if the drug is going to work in humans," Hay says. "But if we don't do a study like this, we won't know if it will work or not."

As it stands now, there are no effective treatments for cognitive impairments, including memory loss.

Provided by University of Arizona