Scientists identify key area that could sever communication between brain and heart in disease

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A team of neuroscientists and anaesthetists, who have been using pioneering techniques to study how the brain regulates the heart, has identified a crucial part of the nervous system whose malfunction may account for an increased risk of death from heart failure. The findings, published online (ahead of print) in the *Journal of Physiology*, could lead to more targeted therapies to help reduce serious illness and death in cardiovascular disease.

The research team, led by Dr Tony Pickering and Professor Julian Paton from the University of Bristol and colleague Professor Robin McAllen from the Florey Neuroscience Institute in Melbourne, developed novel methods which enabled them to explore the activity of nerve cells as they control the beating heart.

The brain controls the heart through two divisions of the nervous system; parasympathetic (vagal) and sympathetic nerves. One of these nerves, the vagus, acts to slow heart rate as part of protective cardiovascular reflexes, which are vital for cardiac health. A loss of vagal control is a major risk factor in human cardiovascular diseases such as heart failure and hypertension.

Vagal information to the heart is transmitted through a special group of nerve cells that remarkably lie on and within the beating heart muscle. Until now, these important neurones have proved especially difficult to

access and record in a system with preserved natural connections. However, academics at the Bristol Heart Institute and Bristol Neuroscience have developed a novel technique that allows the neurones to be held stable while the heart is still beating and their central neural connectivity remains intact.

Using this method the researchers were able to produce high-precision recordings from the cardiac ganglion neurones on the surface of the beating heart whilst retaining their inputs from the nervous system.

The results reveal how these neurones process their inputs and demonstrate that the ganglion plays a key role in regulating the level of vagal tone reaching the heart. This identifies the cardiac ganglion as a site at which the vagal transmission may fail and therefore a potential target for interventions to restore vagal control in cardiovascular diseases.

Dr Pickering, Wellcome Senior Clinical Research Fellow, Reader in Neuroscience and Consultant in Anaesthesia in the University of Bristol's School of Physiology and Pharmacology, said: "These findings are important because they clearly show the cardiac ganglion as a key player in determining the level of vagal tone reaching the heart.

"As loss of vagal tone is found in a number of cardiovascular diseases such as heart failure, following heart attack, in high blood pressure and diabetes, and is associated with poor prognosis and an increased risk of death, our results indicate that therapies targeted at the cardiac ganglion could restore vagal tone and potentially improve outcomes."

Helene Wilson, Research Advisor at the British Heart Foundation (BHF), said: "The vagus nerves are absolutely vital for the control of the speed and regularity of our heart's beat. We don't know a great deal about how the vagus nerves exert this control, and researchers have

found it very hard to study it - partly because of the motion of the heart as it beats. These researchers have now developed a technique to study the processes in an intact vagus nerve which is still attached to heart, and have already helped us understand the process better. New insights into how the vagus nerves transmit their effects on the heart could lead to important new ways to treat patients with diseases such as heart failure, arrhythmias and hypertension."

Provided by University of Bristol